CLINICAL COMPARISON OF THE EFFICACY OF A HERBAL CREAM FOR THE MANAGEMENT OF RADIODERMATITIS IN CANCER PATIENTS

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ABBREVIATIONS

ALL	Acute lymphoblastic leukemia
AML	Acute myelogenous leukemia
CLL	Chronic lymphocytic leukemia
SLL	Small lymphocytic lymphoma
CML	Chronic myelogenous leukemia
AMOL	Acute monocytic leukemia
ASR(W)	Age standardization rate world wide
CIS	Carcinoma *In Situ*
LCIS	Lobular carcinoma *In Situ*
DCIS	Ductal carcinoma *In Situ*
IBC	Invasive breast carcinoma
ILC	Invasive lobular carcinoma
IDC	Invasive ductal carcinoma
NCCN	National Comprehensive Cancer Network
BCT	Breast conservation therapy
CIN	Cervical intraepithelial neoplasia
FAP	Familial adenomatous polyposis
HNPCC	Hereditary non-polyposis colorectal cancer
FOBT	Fecal occult blood test
FIT	Fecal immunochemical test
sDNA test	Stool DNA test
HCV	*Hepatitis C virus*

HBV	*Hepatitis B virus*
SCLC	Small cell lung cancer
NSCLC	Non-small cell lung cancer
SCC	Squamous cell carcinoma
LCC	Large cell carcinoma
PSA	Prostate specific antigen test
TURP	Transurethral resection of the prostate
GIST	Gastrointestinal stromal tumor
CA 125	Cancer antigen 125 test
MRI	Magnetic resonance imaging
FNA	Fine needle aspiration
CNB	Core needle biopsy
BRM	Biological response modifiers
IL-2	Interleukin-2
IFN	Alpha interferon
SERMs	Selective estrogen receptor modulators
SARMs	Selective androgen receptor modulators
CAM	Complementary and alternative medicine
ARA-C	Arabinosylcytosine
IMRT	Intensity modulated radiation therapy
Gy	gray
RTOG	Radiation Therapy Oncology Group
NCI	National Cancer Institute

1. INTRODUCTION

CANCER

Cancer is a class of disease in which a group of cells display uncontrolled growth, invasion that intrudes upon and destroys the adjacent tissues, and sometimes metastasis, or spreading to the other locations in the body via lymph or blood.

Classification

Types of tumour (National Cancer Institute 2008):

Cancers are classified by the type of cell that the tumor resembles and is therefore presumed to be the origin of the tumor. These types include:

- Carcinoma: Cancer derived from epithelial cells. This group includes many of the most common cancers, including those of the breast, prostate, lung and colon.
- Sarcoma: Cancer derived from connective tissue, or mesenchymal cells.
- Lymphoma and leukemia: Cancer derived from hematopoietic (blood-forming) cells.
- Germ cell tumor: Cancer derived from pluripotent cells. In adults these are most often found in the testicle and ovary, but are more common in babies and young children.
- Blastoma: Cancer derived from immature "precursor" or embryonic tissue. These are also commonest in children.

Cancers are usually named using -carcinoma, -sarcoma or -blastoma as a suffix, with the Latin or Greek word for the organ or tissue of origin as the root.

Types of malignancies:

Type of hematological malignancy:
(National Cancer Institute, 2008)

Leukemias

- Acute lymphoblastic leukemia (ALL)
- Acute myelogenous leukemia (AML)
- Chronic lymphocytic leukemia (CLL)
- Small lymphocytic lymphoma (SLL)
- Chronic myelogenous leukemia (CML)
- Acute monocytic leukemia (AMOL)
- Other leukemias

Lymphomas

- Hodgkin's lymphomas (all four subtypes)
- Non-Hodgkin's lymphomas (all subtypes)

Myelomas

Indian Estimated age-standardized incidence and mortality rates: both sexes (World Health Organization-International Agency for Research on Cancer; 2008)

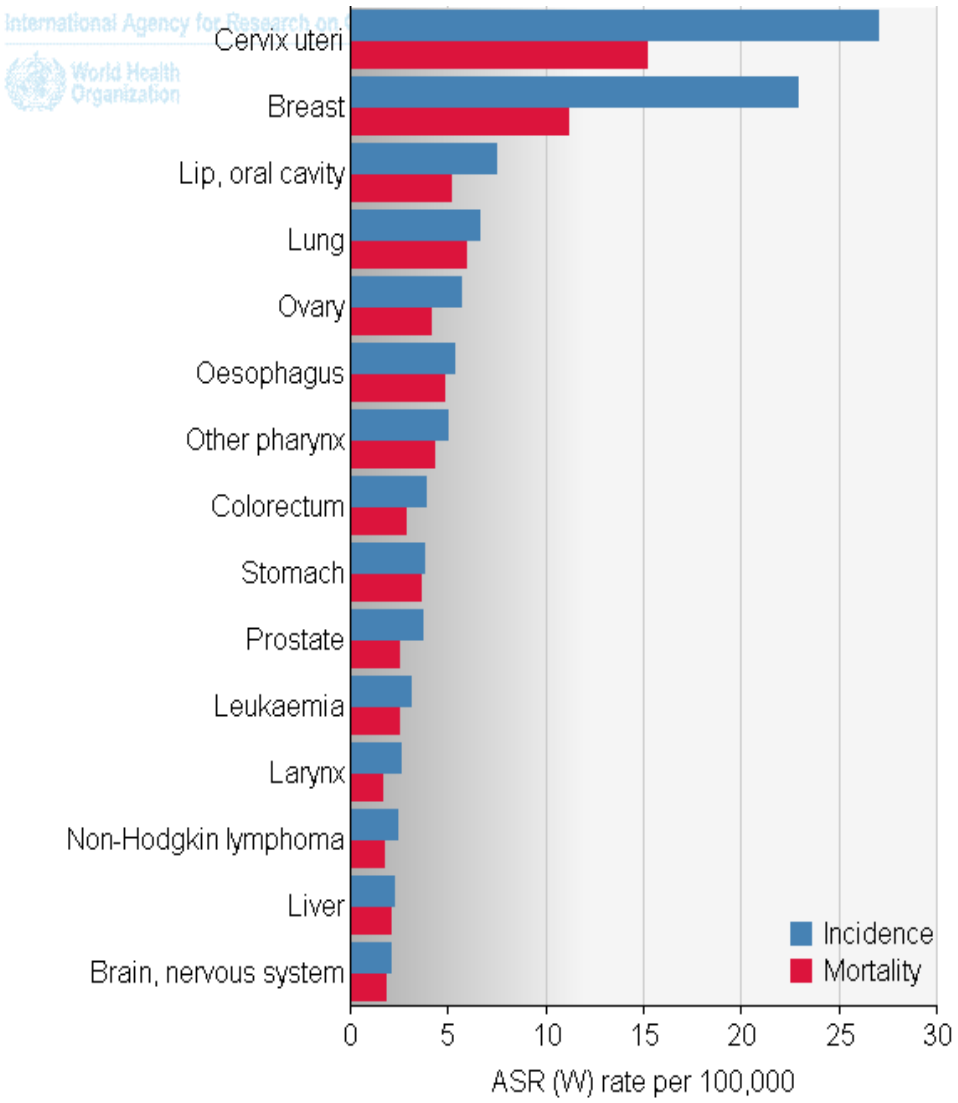


FIGURE: 1

Table: 1

Estimated incidence, mortality and 5-year prevalence: both sexes ASR (W) and proportions per 100,000

Cancer	Incidence		Mortality		5-year prevalence	
	Number	ASR (W)	Number	ASR (W)	Number	ASR (W)
Lip, oral cavity	69820	7.5	47653	5.2	107690	13.4
Nasopharynx	3333	0.3	2412	0.2	8410	1.0
Other pharynx	45271	5.0	39346	4.3	66391	8.2
Oesophagus	48099	5.3	43351	4.8	25610	3.2
Stomach	35059	3.8	33564	3.6	25257	3.1
Colorectum	36476	3.9	25690	2.8	49122	6.1
Liver	20144	2.2	18043	2.0	9639	1.2
Gallbladder	17262	1.9	10279	1.1	21038	2.6
Pancreas	8960	1.0	7766	0.9	5052	0.6
Larynx	23058	2.5	14794	1.7	45753	5.7
Lung	58567	6.6	52269	5.9	26994	3.3
Melanoma of skin	945	0.1	483	0.1	2394	0.3
Breast	115251	22.9	53592	11.1	315679	80.6
Cervix uteri	134420	27.0	72825	15.2	338010	86.3
Corpus uteri	8772	1.9	4851	1.1	32013	8.2
Ovary	28080	5.7	19558	4.1	57796	14.8
Prostate	14630	3.7	10422	2.5	48892	11.8
Testis	3864	0.6	1665	0.3	12980	3.1
Kidney	8900	0.9	5733	0.6	18356	2.3
Bladder	14812	1.7	8203	1.0	33590	4.2
Brain, nervous system	21835	2.1	17941	1.8	31781	3.9
Thyroid	12899	1.2	3029	0.3	51521	6.4
Hodgkin lymphoma	7371	0.7	3587	0.4	11899	1.5
Non-Hodgkin lymphoma	23718	2.4	16243	1.7	27031	3.3
Multiple myeloma	6789	0.8	5941	0.7	11602	1.4
Leukaemia	33307	3.0	26282	2.5	24658	3.1
All cancers	948858	98.5	633455	68.0	1705085	211.4

Signs and symptoms

Symptoms of cancer metastasis depend on the location of the tumor.

Cancer symptoms can be divided into three groups:

- **Local symptoms** are restricted to the site of the primary cancer. They can include lumps or swelling (tumor), hemorrhage (bleeding from the skin, mouth or anus), ulceration and pain. Although local pain commonly occurs in advanced cancer, the initial swelling is often painless.

- **Metastatic symptoms** are due to the spread of cancer to other locations in the body. They can include enlarged lymph nodes (which can be felt or sometimes seen under the skin), hepatomegaly (enlarged liver) or splenomegaly (enlarged spleen) which can be felt in the abdomen, pain or fracture of affected bones, and neurological symptoms.

- **Systemic symptoms** occur due to distant effects of the cancer that are not related to direct or metastatic spread. Some of these effects can include weight loss (poor appetite and cachexia), fatigue, excessive sweating (especially night sweats), anemia (low blood count) and other specific conditions termed paraneoplastic phenomena. These may be mediated by immunological or hormonal signals from the cancer cells.

RISK FACTORS (P. N. Bennett et al., 2001):

The most common cancer risk factors are:

- **Genetic predisposition** -- Certain types of cancer, such as colon and breast cancer often run in families. It is only the predisposition to cancer that is inherited.
- **Estrogen exposure (women)** -- A woman is at increased risk for some gynecological cancers (e.g. breast or uterine cancer) if her system is exposed to too much estrogen, as this stimulates cell proliferation in these tissues.
- **Ionizing radiation** -- Overexposure to ionizing radiation, such as X rays and nuclear radiation can cause DNA injury that may lead to cancer.
- **Ultraviolet radiation** – It is the radiation from the sun. Ultraviolet B (UVB) rays damage cell DNA and cause 90 percent of all skin cancers.
- **Carcinogenic chemicals** -- Chemical carcinogens such as asbestos, benzene, formaldehyde, and diesel exhaust are dangerous in high concentrations.
- **Tobacco smoke** -- Smoking causes 30 percent of all cancer deaths in the United States, making tobacco smoke the single most lethal carcinogen. Smoking can cause cancers in the lungs and other organs.
- **Alcohol** -- People who drink alcohol heavily have a higher risk of mouth, throat, esophagus, stomach, and liver cancer.
- **Carcinogenic foods** -- There are certain foods that contain carcinogens. Foods that should be limited include salted, pickled,

and smoked foods, such as pickles or smoked fish, and meats treated with nitrites.

- **Free radicals** are dangerous, highly reactive chemical compounds that can damage DNA and lead to cancer.

Table: 2

List of Carcinogens and the Cancers

Agent	Cancer Type
Benzo [a]-pyrene (Tobacco)	Lung
Alcohol	Mouth, Pharynx, Larynx, Espohagus
Dietary Fat	Breast
Asbestos	Respiratory-tract, Pleural and Peritoneal Mesothelioma
Fermented Foods	Stomach
Estrogens	Endometrial, Ovarian, Breast
UV Light	Skin
X-Radiation and Gamma Radiation	Leukemia, Thyroid, Breast, Lung, Mouth, Stomach, Colon, Bladder, Ovarian, Skin, Central Nervous System
Tamoxifen	Endometrial
In-Utero Diethylstilbestrol	Childhood Cancer
Transabdominal Radiation	Childhood Cancer
Aflatoxin	Liver
Soot, Coal (Chimney Sweeping)	Scrotal
Nickel (Nickel Refining)	Lung, Nasal
Wood Dust (Woodworking)	Nasal
Cr(VI) (Leatherworking)	Lung
Mustard Gas	Respiratory-tract, Lung
2-napthylamine	Bladder

Origins of Cancer

All cancers begin in cells, the body's basic unit of life. To understand cancer, it's helpful to know what happens when normal cells become cancer cells. The body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are needed to keep the body healthy. When cells become old or damaged, they die and are replaced with new cells.

However, sometimes this orderly process goes wrong. The genetic material (DNA) of a cell can become damaged or changed, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor.

Not all tumors are cancerous; tumors can be benign or malignant.

- **Benign tumors** aren't cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumors do not spread to other parts of the body.
- **Malignant tumors** are cancerous. Cells in these tumors can invade nearby tissues and spread to other parts of the body. The spread of cancer from one part of the body to another is called metastasis.

Some cancers do not form tumors. For example, leukemia is a cancer of the bone marrow and blood **(Robbins's et al., 1999)**.

Pathophysiology

Cancers are caused by a series of mutations. Each mutation alters the behavior of the cell. Cancer is fundamentally a disease of failure of regulation of tissue growth. In order for a normal cell to transform into a cancer cell, the genes which regulate cell growth and differentiation must be altered.

The affected genes are divided into two broad categories. Oncogenes are genes which promote cell growth and reproduction. Tumor suppressor genes are genes which inhibit cell division and survival.

Malignant transformation can occur through the formation of novel oncogenes, the inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in many genes are required to transform a normal cell into a cancer cell.

The Stages of the Cell Cycle

The stages of the cell cycle are depicted below.

- **G1** and **G2** stand for 'gaps'. This refers to the fact that nothing very obvious is occurring in the nucleus of the cells during these stages. The cells are actually very active. They are growing and preparing to divide.
- **S** stands for synthesis. This is the phase of the cell cycle in which the DNA is copied or replicated.

- **M** stands for mitosis. This is the stage of the cell cycle in which the cell actually divides into two daughter cells.

DNA replication occurs in the synthesis or S phase of the Cell Cycle. Every chromosome is copied with high fidelity in a process that involves a large number of enzymes **(Sawant et al., 2003)**.

Characteristics of Cancer Cells

There are numerous changes that must occur for a normal cell to become a cancer cell. Additional changes are needed for that single cell to form a tumor and then for that tumor to grow and spread **(Hanahan D., 2000).**

- Growth Without 'GO' Signals
- Failure to Respond to 'STOP' Signals
- Unlimited Number of Cell Divisions
- Avoidance of Cell Death
- Angiogenesis
- Tissue Invasion and Metastasis

TYPES OF CANCER

The common types of Cancers are,

- Breast
- Cervical
- Colon & Rectal (Colorectal)
- Leukemia
- Liver
- Lung
- Lymphoma

- Multiple Myeloma
- Pancreatic
- Prostate
- Skin
- Stomach (Gastric)

Breast Cancer: Introduction

Breast cancer ranks as one of the leading cancer types in the number of new cases diagnosed. In 2010 the American Cancer Society estimates approximately 209,060 new cases of breast cancer will be diagnosed and 40,230 deaths due to breast cancer will occur in the United States **(American Cancer Society Cancer Facts and Figures 2010).**

Breast Cancer: Types

There are several different kinds of breast cancer. However, the majority of breast cancer cases are classified as either *in situ* or invasive **(Simpson PT et al., 2003).**

Carcinoma *In Situ* (CIS)

- **Lobular Carcinoma *In Situ* (LCIS)**

  Lobular carcinoma *in situ* describes breast cancer that is confined to the **milk-producing glands** (lobules) of the breast.
- **Ductal Carcinoma *In Situ* (DCIS)**

  Ductal carcinoma *in situ* describes breast cancer that is confined to the **milk ducts** of the breast.

Invasive Breast Carcinoma (IBC)

- **Invasive Lobular Carcinoma (ILC)**

  Invasive lobular carcinoma develops in the **milk-producing glands** (lobules) of the breast.

- **Invasive Ductal Carcinoma (IDC)**

  Invasive ductal carcinoma is the most common type of invasive breast cancer, responsible for almost 85% of cases.

Breast Cancer: Risk Factors (Singletary SE et al., 2003)

- Prior History of Breast Disease
- Family History of Breast Disease
- Age
- Race
- Reproductive and Menstrual History
- Hormone Replacement Therapy
- Exposure to Diethylstilbestrol
- Radiation Exposure
- Dietary Factors

Breast Cancer: Symptoms

The American Cancer Society lists the following symptoms associated with breast cancer:

- Presence of a lump or thickening in the breast;
- Swelling, dimpling, redness, or soreness of skin;
- Change in shape or appearance of the nipple; and
- Nipple discharge.

Breast Cancer: Detection and Diagnosis

The American Cancer Society has published guidelines for screening for women with a normal risk for breast cancer.

Detection

- Breast Exam
- Mammography
- Ultrasound
- Breast MRI

Diagnosis

- Fine Needle Aspiration
- Core Needle Biopsy
- Breast Tumor Pathology
- Sentinel Lymph Node Biopsy

Breast Cancer: Treatment

The National Comprehensive Cancer Network (NCCN) lists the following treatments for breast cancer:

- Surgery
- Radiation Therapy
- Chemotherapy
- Hormone Therapy
  - SERMs
- Monoclonal Antibody Therapy
  - Herceptin
- Prophylactic Mastectomy
- Breast Conservation Therapy(BCT)
- Mastectomy

Cervical Cancer: Introduction

Cervical cancer forms in the interior lining of the cervix, the junction of the vagina and uterus. In 2010 the American Cancer Society estimates 12,200 women will be diagnosed with invasive cervical cancer and 4,210 will die of the disease in the United States **(Schiffman M et al., 2007)**

Types of Cervical Cancer (National Cancer Institute)

The two types of cervical cancer are

- squamous cell carcinoma
- adenocarcinoma

Both squamous cell and adenocarcinoma begin in the cells that line hollow organs, but squamous cells have a thin, flat appearance while adenocarcinomas involve cells with secretory functions. Squamous cell carcinoma is far more common and makes up approximately 90% of cervical carcinoma cases.

Cervical Cancer: Risk Factors (Khan MJ et al., 2005)

- Human Papillomavirus (HPV) Infection
- Family History of Cervical Cancer
- Age
- Sexual and Reproductive History
- Socioeconomic Status
- Smoking
- HIV Infection
- *In Utero* DES Exposure
- Long-term use of oral contraceptives

Cervical Cancer: Symptoms (Petignat P et al., 2007)

Typically, early cervical cancer is asymptomatic, but abnormal vaginal bleeding can occur once the cancer becomes invasive.

Cervical Cancer: Detection and Diagnosis

Detection:

- CA-125 for detecting ovarian cancer.
- Pap smear for detecting cervical and vaginal cancer.
- Ultrasound for detecting ovarian and uterine cancer.

Diagnosis:

- Human Papillomavirus Infection
- Cervical Intraepithelial Neoplasia (CIN)
- Colposcopy
- Biopsy

Cervical Cancer: Pathology Report and Staging

Cervical intraepithelial neoplasia (CIN) is an abnormal condition that is detectable by Pap smears and other cervical exams. CIN is the growth of abnormal cells in the lining of the cervix. The image shows microscopic images of normal cervical tissue, CIN 1, CIN 2 and CIN 3.

Cervical Cancer: Treatment (Petignat P et al., 2007)

- Surgery
- Radiation
- Chemotherapy
- Cervical Cancer Vaccine

Colon and Rectal Cancer: Introduction

Colon cancer and rectal cancer, collectively known as colorectal cancer, have many similar characteristics. Colorectal cancer is currently the third most common cancer in both men and women.

In 2010, the American Cancer Society estimates that there will be approximately 142,570 new cases diagnosed and 51,370 deaths due to colorectal cancer in the United States. **(Cancer Facts and Figures 2010. American Cancer Society)**

Colon and Rectal Cancer: Risk Factors

- Family History of Colorectal Cancer
- Age
- Diets rich in red or processed meat
- Excessive drinking of alcohol
- Obesity
- Smoking

The two major colorectal cancer susceptibility syndromes are called

- Familial adenomatous polyposis (FAP)- *Figure shows the mucosal surface of the colon carpeted with numerous early adenomas.*
- Hereditary non-polyposis colorectal cancer (HNPCC)

Colon and Rectal Cancer: Symptoms

- Bleeding in the rectum
- Bloody stools
- A change in bowel habits
- Cramps in the colorectal region
- Anemia from the blood loss

Colon and Rectal Cancer: Detection and Diagnosis (Lemon Set al ., 2001)

- Sigmoidoscopy every 5 years, or
- Colonoscopy every 10 years, or
- Double contrast barium enema every 5 years, or
- CT colonography (virtual colonoscopy) every 5 years

Colon and Rectal Cancer: Treatment

- Surgery
- Radiation Therapy
- Chemotherapy

Lung Cancer: Introduction

Lung cancer currently ranks as the leading cause of cancer related deaths in men and women. 2010, the American Cancer Society estimates 222,520 new cases will be diagnosed and 157,300 deaths due to lung cancer will occur in the United States **(Alberg AJ et al., 2005)**

Types of Lung Cancer

Lung cancer is divided into 2 main types:

- Small cell lung cancer (SCLC)
- Non-small cell lung cancer (NSCLC)

Small cell lung cancer (SCLC) accounts for about 14% of all lung cancers.Also known as *oat cell carcinoma* or *small cell undifferentiated carcinoma*, SCLC tends to be aggressive.

Non-small cell lung cancer (NSCLC) is divided into three categories, based on appearance and other characteristics of the cancerous cells:

- Squamous cell carcinoma (SCC)
- Adenocarcinoma
- Large Cell Carcinoma (LCC)

Lung Cancer: Risk Factors

- Smoking (especially cigarettes, pipes, cigars)
- Secondhand smoke and air pollution
- Family history
- Radon
- Asbestos
- Metals like chromium, cadmium, arsenic
- Chronic lung diseases such as tuberculosis

Lung Cancer: Symptoms

- Persistent cough
- Sputum streaked with blood
- Chest pain
- Voice change
- Recurrent pneumonia or bronchitis

Lung Cancer: Detection and Diagnosis (Ganti AK et al., 2006)

- chest x-ray
- chest CT (computer tomography) scan,
- bronchoscopy (insertion of a tube into the bronchi), and
- Sputum cytology (examination of cells in the phlegm).

Lung Cancer: Treatment

The National Comprehensive Cancer Network (NCCN) lists the following;

- Surgery
- Radiation Therapy
- Chemotherapy

Pancreatic Cancer: Introduction

Pancreatic cancer currently carries with it a poor prognosis. The American Cancer Society estimates that in the year 2010, 43,140 people will be diagnosed with pancreatic cancer and there will be 36,800 deaths **(Ghaneh P et al., 2007).**

Types of Pancreatic Cancer

The type of cancer is based on the cell type and location of the tumor in the pancreas. More than 95% of pancreatic cancers are adenocarcinomas of the exocrine pancreas.

- **Adenocarcinoma -** this is cancer of the exocrine cells that line the pancreatic ducts. The majority of pancreatic cancers are this type.
- **Cystic Tumors -** tumors that cause fluid filled sacs in the pancreas. Most are benign.
- **Acinar Cell Cancers -** tumors that form on the ends of the pancreatic ducts in the cells that produce enzymes.
- **Sarcomas -** tumors that form in the connective tissue that bonds together the pancreatic cells. This is very rare.

- **Ampullary Cancers -** cancer that develops in the ampulla of Vater (where pancreatic ducts and bile ducts merge).

Pancreatic Cancer: Risk Factors (AB Lowenfels et al., 2002)

- Age
- Increased Body Mass Index (BMI)
- Smoking
- Diabetes
- Chronic Inflammation

Pancreatic Cancer: Symptoms (R Freelove et al .,2006)

- Jaundice
- Weight Loss
- Pain in the abdomen and back
- Steatorrhoea
- Glucose Intolerance

Pancreatic Cancer: Detection and Diagnosis

- Preoperative imaging done with CT scan or ultrasound to determine location and size of the tumor
- ERCP and biopsy may be used for further evaluation of the tumor

Pancreatic Cancer: Treatment

- Chemotherapy
- Surgical Resection
- Radiation Therapy
- Palliative Care and Pain Management

Prostate Cancer: Introduction

Prostate cancer is a common cancer affecting the lives of millions of men worldwide. In 2010, the American Cancer Society estimates 217,730 new cases will be diagnosed and 32,050 men will die of the disease in the United States.

Prostate Cancer: Risk Factors (Cox B et al ., 2006)

- Age
- Family History of Prostate Cancer
- Race
- Dietary Factors

Prostate Cancer: Symptoms

- Inability to urinate
- Discontinuous or weak urine flow
- Difficulty in starting or stopping urine flow
- Frequent urination, especially at night
- Blood in urine
- Pain or burning with urination
- Continuous back, pelvis, or upper thigh pain

Prostate Cancer: Detection and Diagnosis

- Digital Rectal Examinations
- Prostate Specific Antigen (PSA) Test
- Biopsy

Prostate Cancer: Treatment

- Radical prostatectomy
- Transurethral resection of the prostate (TURP)
- External beam radiation
- Internal radiation: brachytherapy
- Hormone therapy
- Removal of the testicles (orchiectomy)
- Chemotherapy

Introduction to Skin Cancer

Malignancies of the skin are the most commonly diagnosed cancer type worldwide. The foremost cause of skin cancer remains UV radiation from sunlight. Skin cancer may be classified as either non-melanoma skin cancer (cancer types include squamous cell carcinoma and basal cell carcinoma) or melanoma **(Miller AJ et al., 2006).**

Types of Skin Cancer (Holcomb SS et al., 2006)

Skin cancer may be divided into two types: non-melanoma and melanoma.

Nonmelanoma Skin Cancer

There are two major sub-types of non-melanoma skin cancer:

- ***Basal Cell Carcinoma***- The most commonly diagnosed skin cancer
- ***Squamous Cell Carcinoma***- Appears on body parts that experience increased levels of sun exposure such as the face, lips and back.

Melanoma

Melanoma is a cancerous growth of melanocytes and most frequently develops in the skin. There are several types of melanoma that can be categorized based on their appearance, either with the naked eye or microscopically.

- Superficial spreading
- Nodular type lesions
- Acral lentiginous lesions
- Lentigo maligna melanoma

Skin Cancer: Risk Factors

- Ultraviolet Radiation
- Skin Color
- Sun Sensitivity
- Immunosuppression
- Prior Diagnosis
- Family History
- Radiation Therapy
- Chemical Exposure

Skin Cancer: Symptoms and Detection (Rager EL et al .,2005)

- Asymmetry: melanomas tend to be asymmetrical while benign lesions are more rounded and symmetric.
- Borders: Benign lesions are usually regular and flush with the skin while melanomas may have irregular and/or raised borders.

- Color: Melanomas may be tan, black or brown and often include regions of red, white and blue.
- Diameter: In general, melanomas are larger than 6 mm in diameter.
- Evolution: Changes in physical appearance of melanocytic growths are often observed over time and skin marking should be monitored for changes.

Skin Cancer: Treatment (Rubin AI et al., 2005)

- ***Surgical Treatment***

  Excision of a skin cancer lesion is a frequent treatment option. Excision may be curative for diseases that are in stages I or II (localized).

Non-surgical Treatment

Examples of nonsurgical treatment options include:

- Radiotherapy
- Photodynamic Therapy
- Topical Drug Treatments
- Biological Treatments
- Specific Inhibitors

Gastric Cancer: Introduction (Hohenberger P et al., 2003)

Gastric or stomach cancer is relatively rare in the United States and other developed countries. According to the American Cancer Society, it is estimated that in 2010, 21,000 cases of gastric cancer will be diagnosed.

Gastric Cancer: Types

- Gastric adenocarcinoma
- Gastrointestinal Stromal Tumor (GIST)
- Gastrointestinal Leiomyosarcoma
- Gastrointestinal Carcinoid
- Gastrointestinal lymphoma

Gastric Cancer: Risk Factors (Rocco A et al., 2007)

- *Helicobacter pylori* infection
- Diet
- Gender
- Age
- Ethnicity
- Geography

Gastric Cancer: Symptoms (Layke JC et al., 2004)

- Indigestion, stomach discomfort, or heartburn
- Nausea or loss of appetite
- Feeling tired

Late-stage gastric cancers are associated with the following symptoms:

- Blood in the stool or stools that are black in color
- A bloated feeling after eating, even when eating a small amount

Gastric Cancer: Treatment

- Surgery
- Radiation Therapy
- Chemotherapy

Cancer Prevention:

Antioxidants

The possible role of antioxidants in the prevention and treatment of a variety of medical conditions has been very highly publicized. For some diseases, anti-oxidants may well play an important role

Sources and Uses of Antioxidants

There are many good sources of antioxidants including green tea, berries, tomatoes and soy. Antioxidants can be found in many fruits and vegetables because plants produce antioxidants to help protect themselves from free radicals created by radiation from the sun.

Detection and Diagnosis (Graham DYet al., 2010)

Biopsy

A biopsy is the removal of either a portion of a lesion (incisional) or the entire lesion (excisional). The tissue is then sent to a lab where a pathologist will diagnose the sample. There are two categories of biopsies.

Types of Biopsies

There are several different types of biopsy. The type used depends on the goal of the biopsy (i.e. remove the entire lesion or obtain a small sample), the cancer type and the location of the cancer.

1. Incisional

An incisional biopsy removes only a portion of a suspected tumor. This technique is used when a lesion is too large to remove entirely or when the location of the tumor would result in unacceptable amounts of scarring.

2. Excisional

An excisional biopsy removes the entire tumor and some surrounding tissue. If a diagnosis of cancer results, the biopsy will have removed the entire tumor. These biopsies usually produce a scar.
There are various different techniques used for excisional and incisional biopsies. Punch, Shave, and Needle.

- **Punch**

A punch biopsy is used to collect a deep sample of skin and is usually used for large lesions or lesions on the palm, sole, finger/toe, face, and ear.

- **Shave**

A shave biopsy removes the epidermis and a small portion of the dermis. This technique uses a surgical blade or razor to shave off a portion of the skin.

- **Needle**

A needle biopsy is rarely used to obtain skin tissue; it is usually used to remove a sample from internal organs, lymph nodes, or deep skin areas. These techniques involve the use of a small, hollow needle and are sometimes aided by an imaging technique such as x-ray. There

are two types of needle biopsy, fine needle aspiration (FNA) and core needle biopsy (CNB).

Bronchoscopy

Bronchoscopy is the use of a flexible or rigid tube to examine the airways. Bronchoscopy is used to detect and diagnose lung cancer. It is also used to remove airway blockages (i.e. food), to treat bleeding, to deliver radiation to cancerous areas (brachytherapy) and to take small tissue samples (biopsies).

Cancer Antigen 125 (CA 125) Test

CA 125 (cancer antigen 125 or carbohydrate antigen 125) is a glycoprotein that is produced by the uterus, cervix, fallopian tubes, and the lining of the chest and abdomen.

Colonoscopy

Colonoscopy is a diagnostic technique that allows physicians to visually inspect the interior lining of the colon. A colonoscopy allows a doctor to examine the inside of the entire colon for abnormalities, including; intestinal inflammation, ulceration, bleeding, diverticulitis, colitis, colon polyps, and tumors.

Pap test

A pap test can detect pre-cancerous and cancerous cells in the vagina and cervix. The cervix is the lower part of the uterus that connects the vagina with the main part of the uterus. In a Pap test a small sample of cells is removed from the cervix with a brush or

spatula. The image below shows the process. The procedure is not painful as only the surface of the cervix is touched. The cells are then smeared onto a slide and examined under a microscope. A Pap test can identify abnormal cells and detect changes before cancer has fully developed.

Breast Exam

Breast exams are the first step in early detection of breast cancer. The American Cancer Society recommends:

- women over 20 should do a monthly breast self exam
- women in 20's and 30's should have a clinical breast exam every 3 years
- women over 40 should have a clinical breast exam yearly

Self Breast Exam

A self breast exam involves looking at and feeling your breasts to detect any abnormalities or changes.

Clinical Breast Exam

Clinical breast exams should be done by a physician, nurse practitioner, or other specially trained medical professional who is well trained in the technique during a routine medical exam.

Mammography

It is recommended that women age 40 and older have regular mammograms. Screening is important because the earlier cancer is detected the better the chances are for successful treatment and survival. When detection occurs before any spread, the five-year

survival rate is 97%. After spread to the local lymph nodes, it is 76%. After metastasis to other organs, the five-year survival rate is 20%. The image showed is a labeled representation of a mammography machine.

Ultrasound Imaging

Ultrasound, also called ultrasound scanning or sonography is an imaging method that uses sound waves to create an image of a part of the body. Unlike mammograms, which use radiation (x-rays), ultrasounds expose the body region of interest to high-frequency sound waves.

The computer collects the echoes and creates an image on the screen. In creating the final image, the computer analyzes several characteristics of the returned sound waves:

- **Amplitude**: strength of the signal
- **Frequency**: the number of waves received per second
- **Time Delay**: the time it takes for the signal to return from the targeted region to the transducer.

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is a non-invasive way to view organs, tissues, bones, and other structures inside the body. It uses strong magnetic fields and radio waves to produce internal images of the body. An MRI machine is a large, cylinder shaped machine that contains a very strong donut-shaped magnet. Magnets are commonly measured using gauss and an MRI magnet can be up to 20,000 gauss (common refrigerator magnets are around 10 gauss).

Fine Needle Aspiration (FNA)

A FNA is a type of biopsy. In a biopsy a small sample of tissue is removed for examination by a pathologist. The doctors look at the samples under a microscope and may stain the cells with different dyes to help them distinguish between normal and abnormal cells.

Analysis

Samples are sent to a pathologist specially trained in cytology (cellular abnormalities) to be processed and interpreted. The samples are placed on glass slides and stains are used to reveal the details of the cells. The diagnosis will generally come back as one of five options:

- *Benign* - the mass is not of much concern and will not cause any significant problems as long as it remains unchanged.
- *Atypically indeterminate* - a diagnosis cannot be obtained from the sample. Other tests are needed to determine the nature of the lesion.
- *Suspicious/probably malignant* - not a diagnosis of cancer. This lesion should be biopsied with a more complete method to determine whether a malignancy (cancer) is present.
- *Malignant* - a diagnosis of cancer; should be biopsied and tested for exact tumor makeup to prepare for treatment.

Core Needle Biopsy (CNB)

Biopsies are samples of tissue that are removed for closer examination.

Analysis

A core biopsy sample is studied differently than a FNA sample. The larger size of the sample allows the pathologist to look at the way groups of cells are organized instead of looking at individual cells. In CNB a trained pathologist looks for changes associated with a variety of diseases. Because cancer cells are dividing in an abnormal fashion, they make the tissue around them appear disorganized.

Cancer Treatments

The major types of treatment and their objective are described briefly below.

- **Surgery:** Often the first line of treatment for many solid tumors. In cases in which the cancer is detected at an early stage, surgery may be sufficient to cure the patient by removing all cancerous cells. Benign growths may also be removed by surgery.
- **Radiation:** May be used in conjunction with surgery and/or drug treatments. The goal of radiation is to kill the cancer cells directly by damaging them with high energy beams.
- **Chemotherapy:** A term used for a wide array of drugs used to kill cancer cells. Chemotherapy drugs work by damaging the dividing cancer cells and preventing further reproduction.
- **Hormonal Treatments:** These drugs are designed to prevent cancer cell growth by preventing the cells from receiving signals necessary for their continued growth and division.
- **Targeted Therapy:** This class of drugs is relatively new in the treatment of cancer. They work by targeting specific proteins and processes that are limited primarily to cancer cells or that are

much more prevalent in cancer cells. Inhibition of these processes prevents cancer cell growth and division.

- **Antibodies:** This treatment involves the use of antibodies to target cancer cells. While antibodies are naturally occurring proteins in our bodies, the antibodies used in the treatment of cancer have been manufactured for use as drugs.
- **Biological Response Modifiers:** These treatments involve the use of naturally occurring, normal proteins that stimulate the body's own defenses against cancer.
- **Vaccines:** The purpose of cancer vaccines is to stimulate the body's defenses against cancer. Vaccines usually contain proteins found on or produced by cancer cells.
- **Complementary and Alternative Medicines:** These treatment methods are not practiced by conventional western medicine. They can include herbal, animal derived, and mind-body approaches to treating cancer.

Biological Response Modifiers (BRM)

Biological response modifiers are compounds that are used to treat cancer by altering or augmenting naturally occurring processes within the body. Immunotherapy makes use of BRMs to enhance the activity of the immune system to increase the body's natural defense mechanisms against cancer.

The cytokines most frequently used to treat cancer are:

- Interleukin-2 (IL-2)
- Alpha Interferon (IFN)

Bone Marrow Transplant (BMT)

Bone marrow transplant is used to treat several types of cancer and is commonly used for leukemias, lymphomas and other blood cell cancers. BMT may also be used to treat patients with solid tumors.

Chemotherapy (Lippincott's et al., 1999)

The term chemotherapy or chemo refers to a wide range of drugs used to treat cancer. These drugs usually work by killing dividing cells. Since cancer cells have lost many of the regulatory functions present in normal cells, they will continue to attempt to divide when other cells do not.

- **Antimetabolite:** Drugs that interfere with the formation of key bio-molecules within the cell including nucleotides, the building blocks of DNA. These drugs ultimately interfere with DNA replication and therefore cell division.
- **Genotoxic Drugs:** Drugs that damage DNA. By causing DNA damage, these agents interfere with DNA replication, and cell division.
- **Spindle Inhibitors:** These agents prevent proper cell division by interfering with the cytoskeletal components that enable one cell to divide into two.

Antimetabolites

Many of the antimetabolites used in the treatment of cancer interfere with the production of the nucleic acids, RNA and DNA.If new DNA cannot be made, cells are unable to divide. There are several

different cellular targets for antimetabolites. Some common classes of antimetabolites are:

- Folate Antagonists
- Purine Antagonists
- Pyrimidine Antagonists

Folate Antagonists

Folate antagonists, also known as antifolates, inhibit dihydrofolate reductase (DHFR), an enzyme involved in the formation of nucleotides. When this enzyme is blocked, nucleotides are not formed, which disrupts DNA replication and cell division.

- Methotrexate
- Pemetrexed (Alimta®)

Purine Antagonists

The purines (adenine and guanine) are chemicals used to build the nucleotides of DNA and RNA. The other classes of base, the pyrimidines, are represented in DNA by thymine and cytosine and in RNA by cytosine and uracil.The purine antagonists function by inhibiting DNA synthesis in two different ways:

- 6-Mercaptopurine
- Dacarbazine
- Fludarabine

Pyrimidine Antagonists

The pyrimidine antagonists act to block the synthesis of pyrimidine containing nucleotides (C and T in DNA; C and U in RNA). The drugs used to block the construction of these nucleotides have structures that are similar to the natural compound. Some pyrimidine antagonists used in cancer therapy are:

- 5-fluorouracil
- Arabinosylcytosine
- Capecitabine
- Gemcitabine
- Decitabine

Genotoxic Drugs

Genotoxic drugs are chemotherapy agents that affect nucleic acids and alter their function. These drugs may directly bind to DNA or they may indirectly lead to DNA damage by affecting enzymes involved in DNA replication.

The genotoxic chemotherapy treatments include:

- **Alkylating agents**: The first class of chemotherapy agents used. These drugs modify the bases of DNA, interfering with DNA replication and transcription and leading to mutations.
- **Intercalating agents**: These drugs wedge themselves into the spaces between the nucleotides in the DNA double helix. They interfere with transcription, replication and induce mutations.

- **Enzyme inhibitors**: These drugs inhibit key enzymes, such as topoisomerases, involved in DNA replication inducing DNA damage.

Cryotherapy (Cryoablation)

Cryotherapy or cryoablation (Cryo is from the Greek for frost or extreme cold. Ablation refers to removal or elimination.) is the use of extreme cold to kill tumor cells. A probe containing an extremely cold fluid is placed inside/on the area to be treated and the tumor (or abnormal growth) is frozen. Cryotherapy can be performed during a open (fully invasive) surgery or the probes can be inserted through the skin in a minimally invasive procedure.

Radiofrequency Ablation (RFA)

It has been known for a long time that normal cellular functions will stop if the temperature is raised to 42°C/108°F, and that large-scale cell death--necrosis--will occur at temperatures above 46°C/115°F. Killing cells with heat presents a possible method of cancer treatment; obviously, measures must be taken to minimize the heating of surrounding healthy cells.

Surgery for Cancer

Surgery is frequently used to remove cancerous growths or obtain small samples of tissue for examination. For several types of cancer, surgical removal of a tumor may be sufficient to cure the patient. The likelihood of a surgical cure is dependent on the size, location, and stage of the disease. When removing a tumor the surgeon

will try to remove as much of the tumor as possible. The tissue removed from the patient will often be examined by a pathologist for signs of tumor cells near the edge of the incision.

Hormonal Cancer Treatments

The hormonal treatments described on the following pages all work by interfering with hormonal signals but they may attack different parts of the pathways involved. The types of hormonal antagonists (and specific drugs) discussed include:

- Selective Estrogen Receptor Modulators (SERMs)
- Aromatase Inhibitors
- Receptor Down-regulators
- Selective Androgen Receptor Modulators (SARMs)

Targeted Therapy

The development of targeted therapy represents an exciting new approach to cancer treatment. A small number of these drugs have already been FDA approved and several others are currently in clinical trials.

- Kinases are enzymes that add phosphate groups onto proteins. Because they control many cellular processes, abnormal activity can result in the development of cancer.
- Angiogenesis Inhibitors, Angiogenesis, the development of blood vessels, is critical to the growth of almost all types of cancer.

- Proteasome Inhibitors, Proteasomes are responsible for the destruction of proteins. Inhibition of proteasome activity be used to treat some types of cancer.

Tumor Vaccines

The aim of tumor vaccines is to stimulate the body's immune system in the fight to recognize and eliminate cancer cells. There are many strategies in immunotherapy; some strategies are considered 'passive' while others are 'active'.

- **Passive immunotherapy** involves giving antibodies or mature T cells to the patient to attack the cancer cells. This type of therapy does not induce permanent change in the patient's own T cells, but may be effective in a variety of cancers including leukemia and breast cancer.
- **Active immunotherapy** strategies include tumor vaccines, because they directly stimulate the patient's own immune cells to have a long-lasting response against the cancer.

There are several broad categories of tumor vaccine strategies:

- Whole cell vaccine
- Antigen therapy vaccines
- Antigen-presenting cell vaccines
- Non-specific therapy and cytokine therapy

Managing Side Effects

Cancer and cancer treatment can cause many side effects; some are easily controlled and others require specialized care.

- Anemia
- Anxiety - ASCO curriculum
- Appetite Loss
- Bleeding and Clotting Problems
- Blocked Intestine or Gastrointestinal Obstruction - ASCO curriculum
- Constipation
- Depression - ASCO curriculum
- Diarrhoea - ASCO curriculum
- Difficulty Swallowing or Dysphagia
- Dry Mouth or Xerostomia
- Edema or Fluid Retention
- Fatigue - ASCO curriculum
- Hair Loss or Alopecia
- Mouth Sores or Mucositis - ASCO curriculum
- Nausea and Vomiting
- Pain - ASCO curriculum
- Sexual Dysfunction - ASCO curriculum
- Skin Reactions to Targeted Therapies
- Taste Changes
- Thrombocytopenia

Cancer Drug Resistance

One of the main causes of failure in the treatment of cancer is the development of drug resistance by the cancer cells. It is possible that more than one of these resistance mechanisms can occur in any given case.

- The Selection of Resistant Cells
- Gene Amplification
- Multiple Drug Resistance
- Blood-Brain Barrier
- Changes in Target Molecules

Cancer Treatment Tables

Cancer is treated with a wide variety of drugs. This section contains the following tables:

- Chemotherapy Drugs
- Hormonal Drugs
- Biological Drugs
- Antibody-based Treatments
- Targeted Therapies
- Complementary and Alternative Medicine (CAM)

Table 3: Chemotherapy Drug Table

Generic Name	Brand Name	Type of Chemotherapy
Arabinosylcytosine (ARA-C), Cytarabine	Cytosar-U®	Antimetabolite
Bleomycin	Blenoxane®	Other
Busulfan	Myleran®	Genotoxic Agent
Capecitabine	Xeloda®	Antimetabolite
Carboplatin	Paraplatin®	Genotoxic Agent
Carmustine	Bicnu®, Gliadel®	Genotoxic Agent
Chlorambucil	Leukeran®	Genotoxic Agent
Cisplatin	Platinol®, IntraDose®(Cisplatin; Collagen; Epinephrine)	Genotoxic Agent
Cyclophosphamide	Cytoxan®, Cytoxan®IV, Neosar®, Procytox®	Genotoxic Agent
Dacarbazine	DTIC-Dome®	Genotoxic Agent or Antimetabolite
Daunorubicin	Cerubidine	Genotoxic Agent
Docetaxel	Taxotere®	Spindle Inhibitor
Doxorubicin	Adriamycin®, Rubex®, Doxil®, Caelyx®, Myocet™	Genotoxic Agent
Epirubicin	Ellence®	Genotoxic Agent
Etoposide	Etopophos®, Vepesid®, Toposar®, VP-16®	Genotoxic Agent
Fludarabine	Fludara®	Antimetabolite

Table 4: Hormonal, Biological and Antibody-based Treatment Tables

Generic Name	Brand Name	Type of Hormonal Treatment
Anastrozole	Arimidex®	Aromatase Inhibitor
Bicalutamide	Casodex®	Exemestane
Flutamide	Eulexin®	Specific Androgen Receptor Modulator(SARM)
Fulvestrant	Faslodex®	Estrogen Receptor Down-Regulator
Megestrol	Megace®	Additional Hormonal Treatments
Tamoxifen	Nolvadex®	Selective Estrogen Receptor Modulator (SERM)

Table 5: Biological Treatments

Generic Name	Brand Name	Type of Drug
Aldesleukin, Interleukin-2	Proleukin®	BRM
Alpha Interferon	Intron®, Roferon®-A	BRM
Imiquimod	Aldara®	BRM
Lenalidomide	Revlimid®	BRM

Table 6: Antibody Treatments

Generic Name	Brand Name	Type of Drug
Alemtuzumab	Campath®	Antibody
Bevacizumab	Avastin®	Antibody
Gemtuzumab	Mylotarg®	Antibody
Ibritumomab	Zevalin®	Antibody
Trastuzumab	Herceptin®	Antibody

Table 7: Targeted Therapies Treatment Table

Generic Name	Brand Name	Mechanism of Action
Asparaginase	Elspar®	Enzyme Activator
Bevacizumab	Avastin®	Angiogenesis Inhibitors
Bexarotene	Targretin®	Drug that affects a Molecular Receptor
Gefitinib	Iressa®	Kinase Inhibitor
Imatinib Mesylate	Gleevec®, Glivec®	Kinase Inhibitor

RADIATION THERAPY

Ionising radiation used in radiotherapy causes damage to all living cells, both normal and malignant. The side effects result from damage to cells. The cells that divide rapidly such as skin, bone marrow and the gastrointestinal mucosa are more quickly affected. Acute radiation reactions occur between 10-14 days from the start of radiotherapy and continue to increase in severity until the completion of treatment.

Goals of Radiation Therapy

There are two possible goals of radiotherapy

1. Curative radiotherapy

2. Palliative therapy

The former is used for the purpose of curing the patient and the patient has to engender a small risk of significant side effects. E.g. In

treatment of early stage of Hodgkin's disease, a small risk of myelitis is encountered. The latter is to ameliorate a specific symptom such as pain, obstruction or bleeding. E.g. to relieve pain from metastasis of a distant primary tumor to a bone, one chooses a dose and technique of radiotherapy sufficient to achieve relief of pain but not enough to a risk of osteo-radio-necrosis.

Types of Cancer Treated by Radiation

- skin and lip
- head and neck
- breast
- cervical and endometrium
- Oral cancers
- prostate
- Hodgkin's disease and local extranodal lymphoma
- seminoma of testis and dysgerminoma of ovary
- medulloblastoma, pineal germinoma,and ependymoma
- retinoblastoma
- choroidal melanoma

Types of Radiation Therapy

Radiation can harm both cancerous and normal tissues, the treatment is based on the fact that fast growing cells, such as those found in tumors, are more sensitive to radiation damage. The radiotherapy technique used depends on the type, extent and location of the cancer, and the goal of treatment.

Internal radiation called brachytherapy is the process of implanting radioactive material onto or near the tumor or placing radioactive sources into the body. It can be temporary or permanent. Depending on the location of the implant the treatment may be handled as either an in- or out-patient procedure.

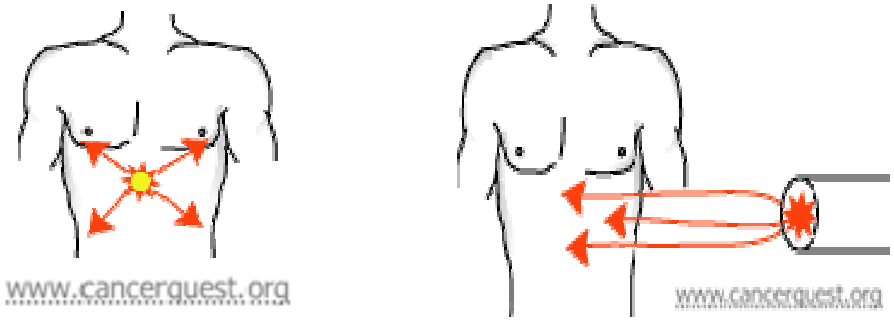


Figure 2: Internal and external radiation

External radiation therapy utilizes a machine to deliver radiation to the tumor. This therapy is primarily an outpatient treatment. Most protocols last approximately 4-7 weeks with treatments given 5 days per week. Both internal and external therapies act to destroy the ability of the cancer cells to reproduce. There are several different types of radiation that may be utilized

Administration of Radiation Therapy

There are several different ways to administer radiation. Some of the more common are listed below. Many new procedures are currently under investigation.

Internal

- *Seed implants*

  This method is most often used to treat prostate cancer. Radioactive seeds are implanted and placed directly on the cancer mass. The seeds are smaller than a grain of rice. Up to 150 seeds may be implanted.

- *Brachytherapy*

  This method is most often used as a local treatment for early stage carcinomas. Sealed radioactive sources are used to deliver radiation to the tumor from a short distance. The two radioactive sources used are 103Pd and 125I.

External

- *External Beam Radiation Therapy* This method uses large machines to produce high and low energy X-ray beams. The amount of radiation required is dependent upon the type of cancer. For example, the level of radiation necessary to destroy a skin carcinoma is less than the amount needed to treat a cancer that is located deep within the body.

- *3-D Conformal Therapy and Intensity Modulated Radiation Therapy (IMRT)*

  This method, which is newer and more precise than external

beam, uses computer imaging to calculate the most efficient dose and combination of radiation treatments.

MECHANISM OF ACTION

Ionizing radiation acts directly and indirectly on viable cells of neoplasm as well as on normal cells near by the lesion **(Perez *et al.*, 2007)**.

One-Third (1/3) of the biological effects of irradiation is by direct damage to cells. It is caused by high energy photons or electrons hitting the cell and changes are brought about within 10^{-10} seconds. RNA and DNA damage are produced by breaking the relatively weak bonds between the nucleic acids. The volume of viable cells which absorb radiation energy is inactivated. As a result of irradiation, DNA damage occurs in normal somatic cells, in reproductive cells and in tumor cells, resulting in radiation induced malignancy, radiation induced congenital anomaly and radiation induced tumor cell apoptosis leading to cell death, respectively.

Two-Third (2/3) of the biological effects of radiation is by the indirect damage to cells. Photons are absorbed by water and cause radiolysis. Water being the predominant molecule in biological system (75%) which interacts and produces changes.

$$H_2O \xrightarrow[\text{Radiation}]{\text{Ionizing}} H_2O^+ + e^- \quad \text{dissociates at once } H^+ + OH^+$$

$H_2O + e^- - H_2O$ - Dissociates at once $H^- + OH^-$

$H^+ + H$ - H_2

$OH^+ + OH$ - H_2O_2

Free radicals H^+, H^-, OH^+, OH^- are unstable. Being highly reactive, they combine with one another and break protein linkages in DNA. These ionizing radiations, which arrest cell division or cause cell death, are used in radiation therapy.

DOSE

Radiation dose selection is a complex issue. Determination of correct number of fraction of radiation per day, the correct dose per fraction, the proposed total dose of irradiation depends on two factors. Factor-1 is the tumor control within radiotherapy field as function of the dose administered. Factor-2 is the normal tissue tolerance, a balancing act between a sufficient dose of radiation to control tumor and not so much dose to cause ill effects.

The amount of radiation used in radiation therapy is measured in gray (Gy), and varies depending on the type and stage of cancer being treated. For curative cases, the typical dose for a solid epithelial tumor ranges from 60 to 80 Gy, while lymphoma tumors are treated with 20 to 40 Gy.

FRACTIONATION

The total dose is fractionated (spread out over time) for several important reasons. Fractionation allows normal cells time to recover,

while tumor cells are generally less efficient in repair between fractions **(Parsons *et al.*, 1988)**. Fractionation also allows tumor cells that were in a relatively radio-resistant phase of the cell cycle during one treatment to cycle into a sensitive phase of the cycle before the next fraction is given. Similarly, tumor cells that were chronically or acutely hypoxic (and therefore more radio resistant) may reoxygenate between fractions, improving the tumor cell kill.

Benefits of Radiation Therapy

- Destroys quickly dividing cells at the margins of tumors. Surgery may miss these cells leading to recurrence of disease.
- Can successfully eradicate growth without permanently damaging the adjacent normal tissue. If these tumors can be treated early before metastasis, there is a very high rate of curability.
- In conjunction with other treatments, may cure tumors that are not responsive to any single agent.
- Radioactive seed implants can deliver high doses of radiation directly to the tumor sparing nearby healthy cells. Has less severe side effects than external radiation therapy.
- Preoperative radiation therapy can kill tumor cells at margins of the tumor site. It can keep the cancer under control and prevent metastases, and also convert technically inoperable tumors into operable ones.
- Postoperative radiation therapy can destroy cancer cells still present around the margins after a tumor has been surgically removed.

Radiation Side Effects

Radiation treatments use high energy waves to damage and kill cancer cells. Because the radiation can affect cells other than cancer cells, side effects may occur. The side effects that any given patient has depend on the type and amount of radiation used and the area being treated.

Possible side effects include:

- Fatigue (in part due to energy expended in replacing normal cells killed in the process)
- Skin irritation, redness, lesions, peeling
- Hair loss
- Loss of taste
- Erectile dysfunction
- Decreased blood count (may be monitored by the clinician overseeing the treatment)
- Increased susceptibility to infection
- Difficulty swallowing and decreased appetite
- Oral mucositis (cells of the mouth rapidly dividing)

Types of Skin Reactions Occur

Radiation-induced skin reactions may progress from erythema (redness), to desquamation (shedding of outer skin layers), and sometimes to ulceration. During the first week or two of radiation treatment, subjects may notice a faint redness and your skin may become itchy or tender. After three to four weeks, skin may become dry

and peel or you may notice moist areas. Later effects of radiation may include darkening or thinning of the skin.

The following are some common reactions that can occur on radiated skin:

- Rash, redness, sunburned-like appearance
- Itching (pruritus), flaking, scaling
- Tenderness, discomfort, pain, burning
- Dryness, peeling
- Blisters, sores, ulcers
- Moist (weeping) areas, oozing
- Swollen, puffiness
- Infection
- Increased sensitivity to sunlight

RISK FACTORS FOR SKIN REACTIONS

Radiosensitivity of tissues varies between individuals and between the various skin structures. A number of factors can affect the potential for skin reactions and include the total dose of radiation given, the location of the area treated and the volume of tissue irradiated. Previous exposure to ultraviolet radiation and increasing age causes the skin to be more fragile and sensitive, along with medical conditions such as diabetes, and immune compromised status and previous surgery. Patients with a poor nutritional status, those who smoke tobacco and on steroid therapy are all in the high risk category **(Turesson et al., 1996) (Harper et al., 2004).**

CHEMOTHERAPY AND RADIATION

Studies have found instances when chemotherapy in association with radiation produces skin changes, and can be classified as acute responding (occurring weeks to months after irradiation and late responding (occurring months to years) after treatment. The simultaneous administration of chemotherapy and radiotherapy can produce an intense skin reaction e.g.

- Doxorubicin may produce skin erythema, vesiculation, desquamation or hyperpigmentation.
- Methotrexate may cause erythema and ulceration.

TOLERABILITY OF RADIATION THERAPY

Full-dose radiation is usually given only once to a particular part of the body. The normal tissues can safely tolerate a limited amount of radiation. Radiation oncologist picks the right dose of radiation to accomplish 2 things:

- To reach the maximum therapeutic dose — the amount that's likely to destroy cancer cells
- To avoid or minimize side effects to the normal tissue

After radiation is over, the normal tissues heal and get back to normal. If cancer returns to the same breast area, depending on the radiation dose you already received, you may or may not be able to receive a limited amount of additional radiation treatment in that same area.

SEQUENCES OF RADIATION THERAPY

The sequence and timing of radiation treatment depends on your individual situation. Radiation may be given immediately after surgery or after other forms of treatment. Here are some examples of various treatment sequences that involve radiation:

- surgery → radiation → possible hormonal therapy
- surgery → chemotherapy → radiation → possible hormonal therapy
- chemotherapy, targeted therapy, or hormonal therapy → surgery → radiation → possible hormonal therapy

RADIODERMATITIS:

Radiodermatitis, also known as radiation dermatitis or radiation skin reaction, is caused by the changes cells undergo in the basal layer of the epidermis and the dermis **(Wickline, 2004).**Up to an estimated 95% of patients receiving radiation therapy will experience some degree of skin reaction, which may include erythema, dry desquamation, and moist desquamation **(De Conno, Ventafridda, & Saita, 1991; King, Nail, Kreamer, Strohl, Johnson, 1985; Porock & Kristjanson, 1999).**

Approximately 95% of radiation oncology patients will experience radiodermatitis and 87% will experience moderate to severe radiodermatitis during or after their therapy **(McQuestion, 2006; Fisher J et al., 2000).**

PATHOPHYSIOLOGY

The skin is the largest organ of the body and is composed of two layers, the epidermis and the dermis. The most superficial layer, the epidermis, is made up of a thin layer (< 2 mm) of keratinized squamous cells that serve as a protective barrier against pathogens and prevent water loss from the body **(McQuestion, 2006).** The dermal layer is slightly thicker (1-3 mm) and contains blood vessels that nourish the skin and assist with thermoregulation **(Harper, Franklin, Jenrette, & Aguero, 2004)**. The dermis also contains nerves that are responsible for sensation, glands that are involved in immune function, and hair follicles **(McQuestion, 2006).** The skin is continually renewing itself. New skin cells proliferate and mature at the dermal layer and migrate to the epidermis over a period of two to three weeks.

The microscopic image of a radio dermatitis lesion given can easily distinguish the thick keratin layer below the epidermis, which would certainly show as an area of increased density on a mammogram, there is no evidence of any malignant cell activity.

Radiodermatitis may be acute or chronic and exists on a continuum of erythema, epilation, desquamation, ulceration, or necrosis. Acute skin changes occur within 90 days of initiating therapy as a result of cytokine-mediated inflammation and DNA damage **(Hymes, Strom, and Fife, 2006; Muller, Khan, Port, Abend, Molls, Ring, & Meineke, 2006).**

- Erythema and swelling may begin within hours or days of initiating radiation therapy due to the release of cytokines that

cause capillary dilation, leukocyte infiltration, and localized swelling **(Hymes, Strom, and Fife, 2006; McQuestion, 2006).**

- Dryness and epilation may occur within days to weeks due to damage of sebaceous glands and hair follicles in the dermal layer **(McQuestion, 2006).**
- Dry desquamation, characterized by dryness, scaling, and pruritus, typically can occur after the third week or after a cumulative dose of 30 Gy due to destruction of regenerative basal cells **(Richardson, Smith, McIntyre, Thomas, & Pilkington, 2005).**
- Dry desquamation typically resolves within one to two weeks of therapy **(McQuestion, 2006).**
- Moist desquamation, evidenced by red, exposed dermis and serous oozing, occurs after four to five weeks of therapy or with 45 to 60 Gy cumulative dose as the basal cells are further depleted **(Richardson et al., 2005).** Acute radiodermatitis usually resolves within three to four weeks after therapy **(McQuestion, 2006).**

Late effects can occur anywhere from 90 days to years after completing therapy as a result of permanent damage to the dermis **(Harper, Franklin, Jenrette, & Aguero, 2004).**

- Late radiation-induced skin changes include atrophy, fibrosis, telangiectasias, and pigmentation changes.
  Radiation destroys fibroblasts in the dermis, resulting in reabsorption of collagen and tissue atrophy **(Harper et al., 2004)**

- Radiation-induced fibrosis is characterized by progressive induration, edema, and thickening of the dermis **(Harper et al., 2004).**
- Radiation also damages the vasculature of the dermal layer and blood vessels become prominent, dilated, and thin, also known as telangiectasias **(Harper et al., 2004).**
- Irradiation exposure may destroy the dermal melanocytes, leading to hypopigmentation, or it may trigger the increased production of melanin in the skin, causing hyperpigmentation **(Harper et al., 2004).**

CLINICAL PRESENTATION

The assessment of radiodermatitis should utilize a validated assessment tool. The Radiation Therapy Oncology Group (RTOG) and the National Cancer Institute (NCI) have established similar assessment tools that classify radiodermatitis by severity. In brief, mild radiodermatitis (RTOG and NCI Grade 1) is characterized by mild, blanchable, erythema or dry desquamation. The onset is typically within days to weeks of initiating therapy and symptoms may fade within a month **(McQuestion, 2006).**

Moderate radiodermatitis (Grade 2) is often painful and presents as edema and moist desquamation that is localized to the skin folds **(Hymes, Strom, & Fife, 2006)**. In severe radiodermatitis (Grade 3 and 4), the area of moist desquamation has spread to areas outside of the skin folds. Grade 4 radiodermatitis indicates that ulcers, hemorrhages, and/or tissue necrosis is present. Ulcers may be red with raised edges

with a red or black base (McQuestion, 2006). Unfortunately, ulceration is very painful and does not heal well **(Gerlach, 2005).**

DIFFERENTIAL DIAGNOSIS

The patient's treatment history, specifically the duration of and cumulative dose of radiotherapy, will provide the best clue as to the diagnosis of radiodermatitis. However, there are several other differential diagnoses to consider that include radiation recall, cellulitis, eczema, and secondary malignancy **(Chen et al, 2009; Yeo & Johnson, 2000).**

Table 8: RTOG SCALE (Radiation Toxicity Oncology Group)

The Radiation Oncology Group (RTOG) produced toxicity criteria which measures skin reactions.This is used in radiotherapy departments and can b e classified into three levels.	
RTOG: 1	Faint or dull erythema with epilation, decreased sweating, drying, reddening,tingling, itching and warmth.
RTOG: 2	Tender or bright erythema with patchy moist desquamation with moderate oedema.
RTOG: 3	Confluent moist desquamation, the inflamed epidermis may slough leaving painful denuded areas of dermis exuding serum.
(Cox J.D. Stetz J. Patak T.F. 1995).	

Table 9: RTOG Radiation Morbidity Scoring

Onset			**Grade**			
	0	1	2	3	4	5
Acute	No change over base-line	Follicular, faint or dull erythema/ epilation/ dry desquamation/ decreased sweating	Tender or Bright erythema. Patchy moist desquamation/ moderate Edema.	Confluent, Moist desquamation Other than skin folds. Pitting edema.	Ulceration. Hemorrhage Necrosis	n/a
Chronic	None	Slight atrophy.	Patch atrophy. Moderate telangiectasia. Total hair loss.	Marked atrophy. Gr oss telangiectasia.	Ulceration	Death

Adapted from Radiation Therapy Oncology Group (2010)

Table 2: NCI Radiation Toxicity

	Grade			
0	1	2	3	4
None	Faint erythema/ dry desquamation	Moderate erythema/ Patchy moist desquamation, confined to skin folds/ moderate edema	Confluent moist Desquamation >1.5 cm, not confined to skin folds/ pitting edema	Ulceration or skin necrosis

Adapted from National Cancer Institute (1999)

IMPROVING PATIENT OUTCOMES

The successful outcome of oral mucositis treatment depends greatly on the patient's proper use of medications. Methods to improve the use of medication can include

- Patient counselling (education)
- Determination of patient compliance with therapy.

PATIENT COUNSELLING (EDUCATION)

Patient counselling may be defined as an interactive session designed to educate the patient about the medication by providing complete information and identifying and removing barrier to appropriate therapy **(Parthasarathy G, 2004)**.

Effective patient counselling aims to produce the following results

- Better patient understanding of their illness and the role of medication in its treatment
- Improved patient compliance
- Reduced incidence of adverse effects and unnecessary healthcare costs
- Improved quality of life for the patient
- Better coping strategies to deal with treatment related adverse effects
- Improved professional rapport between the patient and pharmacist

PATIENT COMPLIANCE

Compliance with medical treatment is one of the most significant global public health concerns facing society today. With cancer particular, there are an ever increasing number of patients burdened with the disease due to the ageing population profile and the social habits. Since the majority of cancer patients are being not aware of the radiation therapy and that its discontinuation may lead to an ineffective treatment, and the recurrence of tumor repopulation. Despite the availability of various treatments to cancer, poor compliance is found to occur due to the illiteracy and economic costs of the treatment.

The term compliance is sometimes used interchangeably with adherence. They both describe the agreement between the medical regimen prescribed by the treating physician and actual patient practice. However, adherence implies a more active role of the patient in the process and indicates a responsibility of both parties to achieve success **(Berg, 1993; Greenburg, 1984)**.

Steps to improve patient compliance

Improving adherence to treatment through patient education is important but not as practical or effective when performed by the physician alone. A multi-disciplinary approach involving the physician, technicians or nurses, social workers and pharmacists may be more effective. The multi-disciplinary intervention involves video- and brochure-based patient education; personalized counselling by a pharmacist, and regular follow-up telephone calls by a pharmacist.

Importance of cancer education

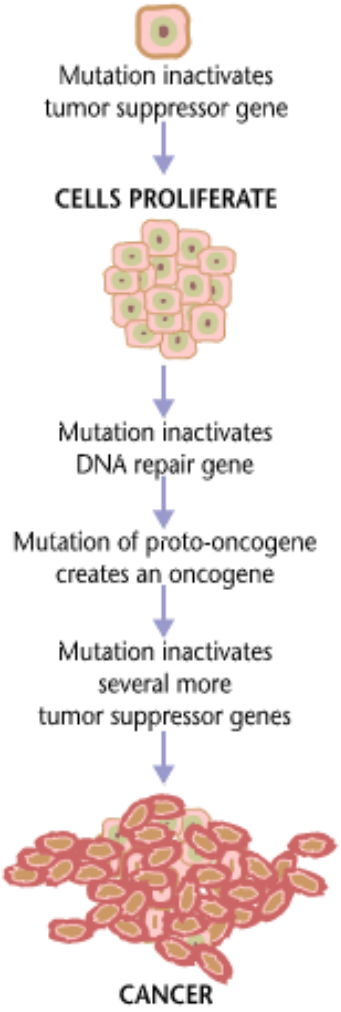
- To create awareness that cancer is not a communicable disease among the relatives of the patients
- To create an awareness about the treatments available to cancers, the beneficial effects that may supersede the side effects of the radiotherapy
- Maintenance of proper oral hygiene during radiotherapy, particularly in case of head and neck cancers
- Need for a planned proper nutritional diet during the radiotherapy treatment E.g.
- To take high protein-rich foods
- To avoid hot and spicy foods
- To take soft foods and liquids that is rich in calories
- Small frequent feedings are recommended when appetite is poor and when swallowing is difficult
- Need for a regular follow up visit, to check for the tumor recurrence
- Tobacco and alcohol use, which contributes to mucosal irritation and tumor repopulation should be strongly discouraged
- Necessary screening and rehabilitation awareness should be created

GENERAL SKIN CARE ADVICE

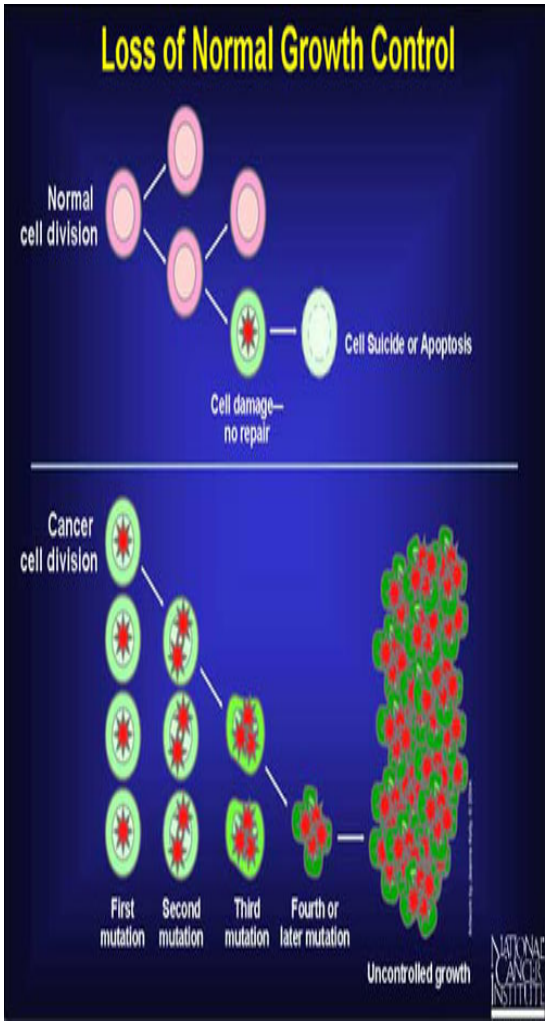
The following skin care guidelines are issued to all patients before the start of radiotherapy, and apply to the area being treated, including both the entry and exit sites.

- Use lukewarm water and a non-perfumed, non-medicated soap.
- Pat dry using a soft cloth, do not rub harshly.
- Do not rub, scratch or scrub the treatment area.
- If the axilla is within the treatment area shaving should be avoided.
- Do not use flannels, loofahs or brushes on the treatment area.
- Do not use perfumed skin products on the treatment area e.g. deodorants, aftershave or perfume.
- Use a mild detergent (fragrance-free if possible) for washing clothing that will be worn next to the treatment area.
- Wear soft loose cotton clothing over the treatment area, avoid straps or belts that may rub
- Following mastectomy, if a permanent prosthesis causes increased friction and /or moisture a soft prosthesis should be used.
- Do not use Elastoplasts or adhesive tape on the treatment area.
- Do not apply heat e.g. hot water bottles or hot / cold packs to the treatment area.

PHOTOGRAPHIC PLATE 1:

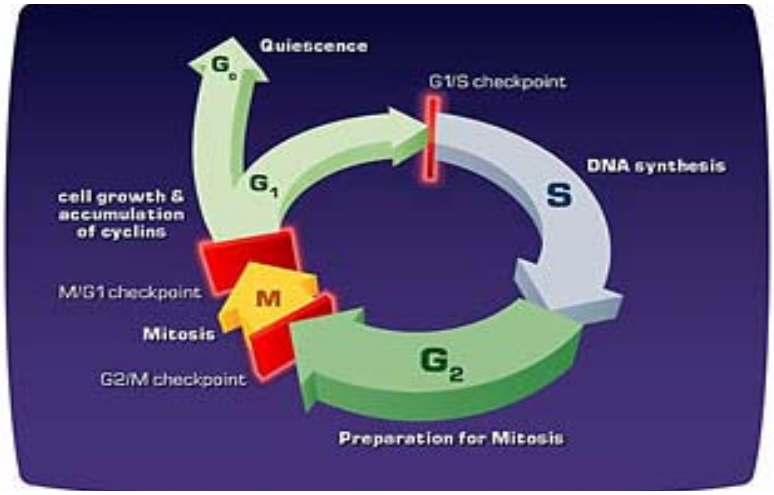


Proliferation of cancer cell

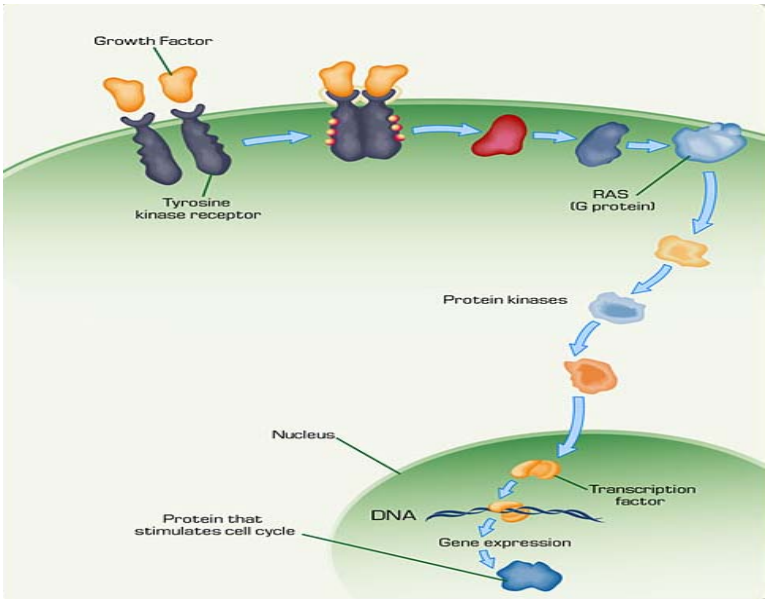


Cell division of normal and cancer cells

PLATE 2:



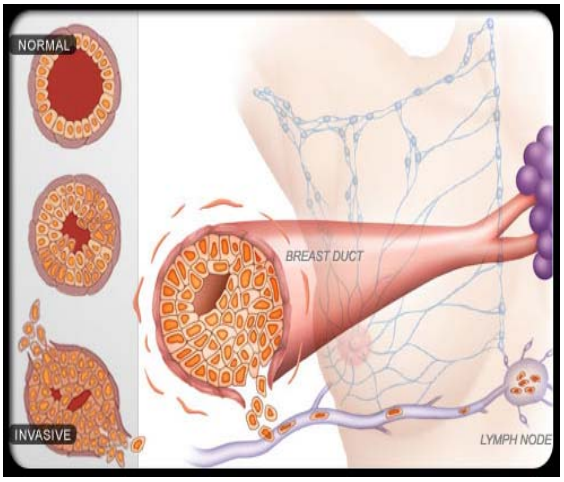
Cell cycle



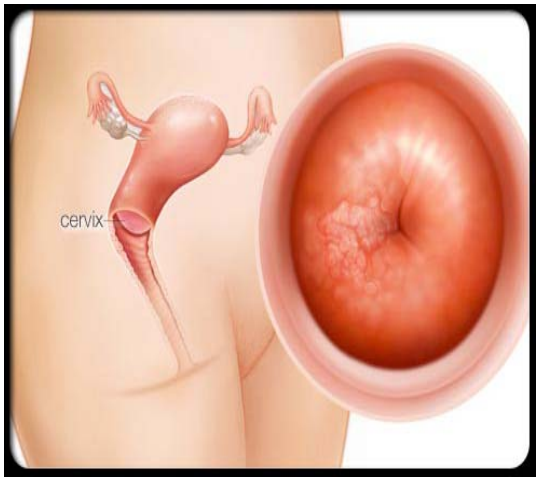
Signal Pathway in the cancer cell

PLATE 3

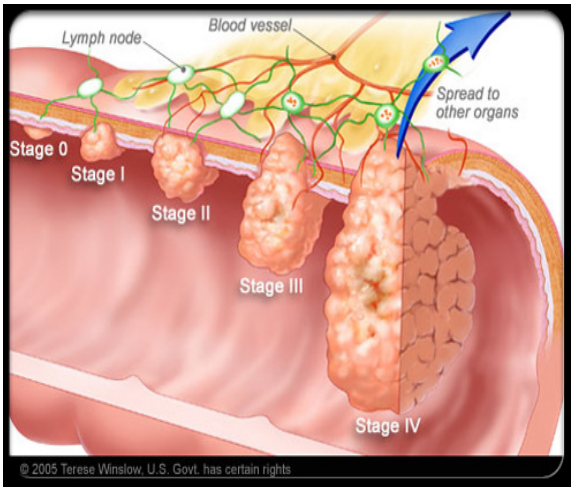
Stages of Breast cancer



Cervix cancer



Colon cancer



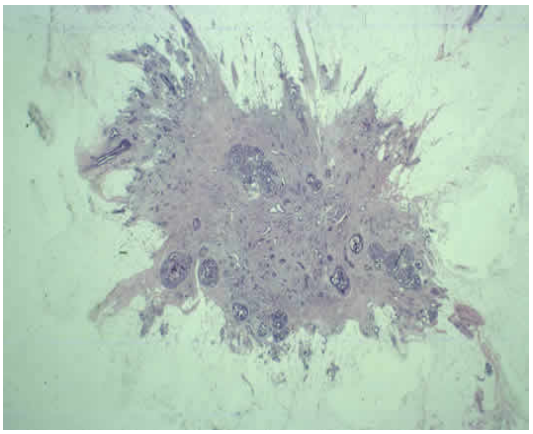
Anatomy of Lungs

PLATE 4

Images of invasive breast cancer:

Left: Pathology slide image of cancerous breast tissue,

Right: Tumor (white area) in fatty breast tissue.



Cervical Intraepithelial Neoplasia

Colon: Familial adenomatous polyposis

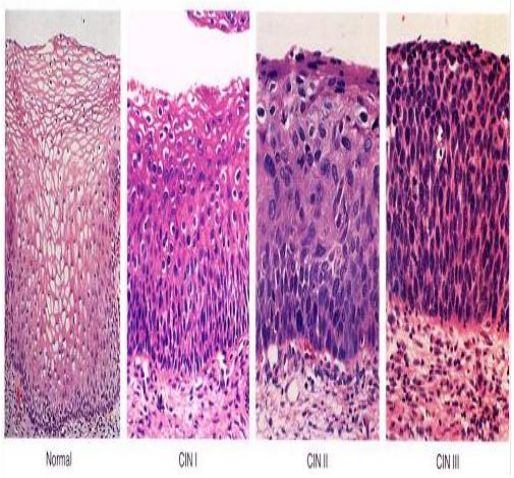
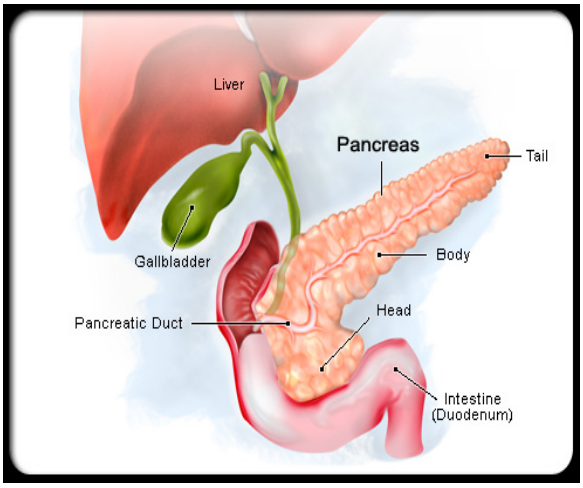
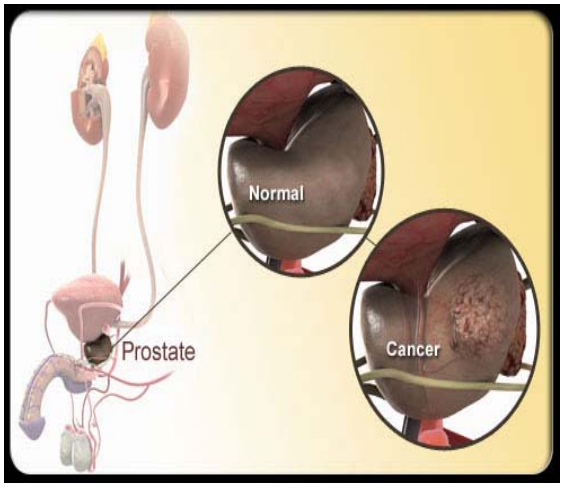


PLATE 5

Pancreas



Prostate cancer



Skin cancer

Gastric cancer

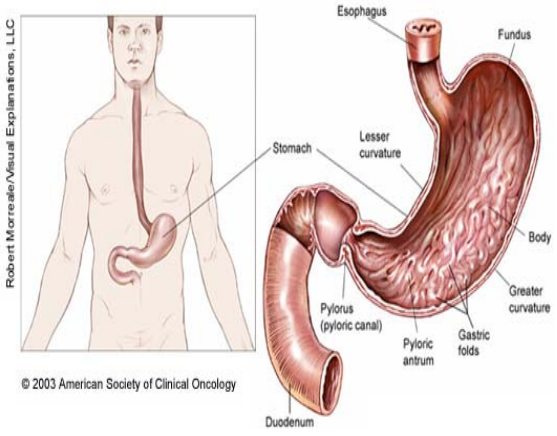
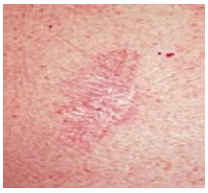


PLATE 6

Basal Cell Carcinoma



Squamous Cell Carcinoma




Skin cancer- symptoms and detection

Asymmetry:

Border:

Color:

Diameter:

Images used courtesy of the Skin Cancer Foundation.

PLATE 7

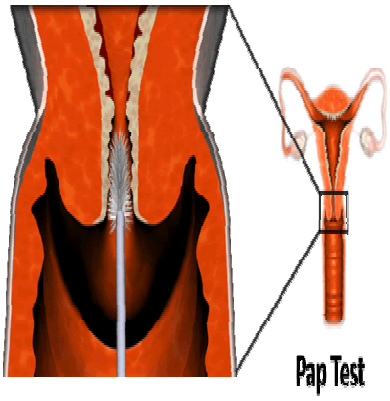
Images of the colonoscope

Normal Colon

Colon with Polyp

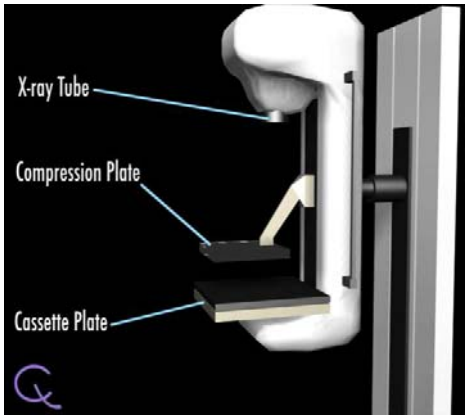
Colon with cancer

Pap test



Ultrasound Imaging

Mammography



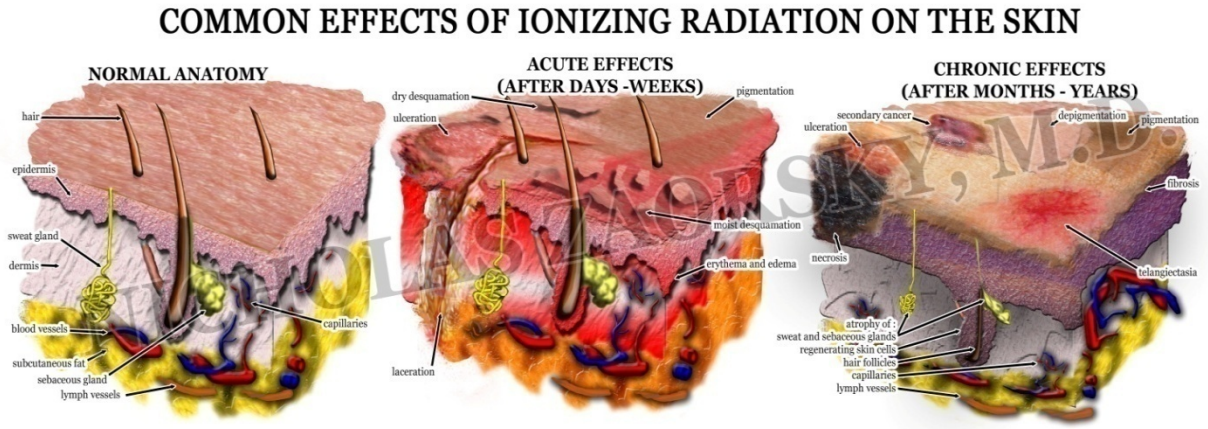
Magnetic Resonance Imaging

PLATE 8

KMC RADIATION UNIT

KMC RADIATION WARD

PLATE 9



Microscopic image of a radio dermatitis lesion

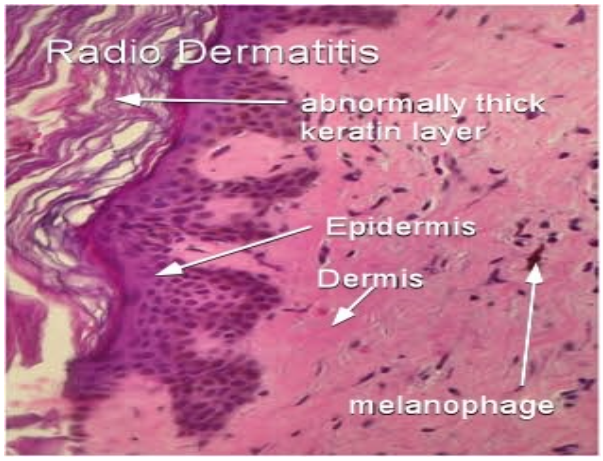


PLATE 10

SKIN REATION APPEARANCE

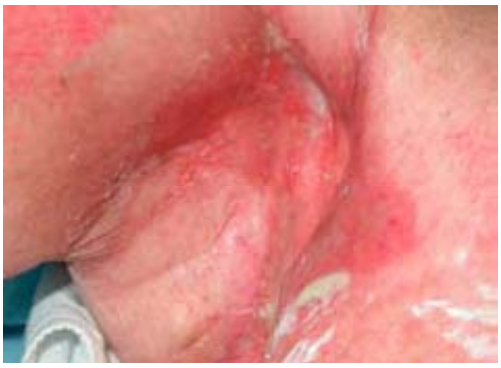
RTOG 1

- Faint or dull erythema

RTOG 2

- Patchy moist desquamation.
- Moderate oedema.

RTOG 3



- Confluent moist desquamation.

2. DRUG PROFILE

Amrad cream contains

- Calendula
- Chamomile
- Aloe vera
- Rubia cordifolia

CALENDULA FLOWER

Figure : 3

Biological Name: Calendula officinalis

Overview:

The flower petals of the calendula plant (*Calendula officinalis*), or pot marigold, have been used for medicinal purposes since at least the 12th century. Calendula is native to Mediterranean countries but is now grown as an ornamental plant throughout the world. However, it is not the same as the annual marigold plant that's often grown in gardens.

Plant Description:

Calendula is an annual plant that thrives in almost any soil but can typically be found in Europe, Western Asia, and the United States. It belongs to the same family as daisies, chrysanthemums, and ragweed. Its branching stems grow to a height of 30 - 60 cm, and it blooms from early spring until frost. The orange-yellow petals of the flowers are used for medicine.

Parts Used:

The dried petals and leaves of the calendula plant are used for medicinal purposes.

Active Compounds:

The flavonoids, found in high amounts in calendula, account for much of its anti-inflammatory activity; triterpene saponins may also be important. Calendula also contains carotenoids.

Medicinal Uses and Indications:

Today, calendula is not usually taken by mouth. The exception is when it is used in extremely small amounts in homeopathic preparations. Calendula is usually applied topically, to the skin

- It was used for treating boils, rashes, inflamed or damaged skin.
- It reduces inflammation, swelling, itching and has antiseptic, astringent actions, and it is effective against acute dermatitis.

Burns, cuts, and bruises

Calendula tinctures, ointments, and washes are often applied to the skin to help burns, bruises, and cuts heal faster, and to fight the minor infections they cause. Calendula cream is also used to treat hemorrhoids.

Dermatitis

Early evidence suggests that calendula may help prevent dermatitis -- skin inflammation -- in breast cancer patients who are undergoing radiation therapy, when compared with another lotion. However, the study wasn't double-blind, meaning the women knew whether they were using calendula or the other lotion.

Available Forms:

Fresh or dried calendula petals are available in tinctures, liquid extracts, infusions, ointments, and creams. Calendula products should always be protected from light and moisture, and should not be used after 3 years of storage.

Pediatric

- Use only topical and homeopathic preparations for children.
- Calendula can be applied to the skin using a 2 - 5% ointment.
- For homeopathic dosages, consult a licensed homeopath.

Adult

- Infusion: 1 tsp (5 - 10 g) dried florets in 8 oz (250 ml) water; steep 10 - 15 minutes; drink 2 - 3 cups per day
- Fluid extract (1:1 in 40% alcohol): 0.5 - 1.0 ml 3 times per day
- Tincture (1:5 in 90% alcohol): 5 - 10 drops (1 - 2 ml) 3 times per day
- Ointment: 2 - 5% calendula; apply 3 - 4 times per day as needed

Precautions:

The use of herbs is a time-honored approach to strengthening the body and treating disease. Herbs, however, can trigger side effects and can interact with other herbs, supplements, or medications. For these reasons, you should take herbs with care, under the supervision of a health care provider.

Possible Interactions:

There are no known scientific reports of interactions between calendula and conventional or herbal medications. In theory, taking calendula orally may interact with the following medications, so talk to your doctor before combining these drugs with calendula:

- Sedatives
- Drugs to treat high blood pressure
- Medications to treat diabetes

Traditional Uses in Herbal Medicine:

Calendula flowers were believed to be useful in reducing inflammation, wound healing, and as an antiseptic. Calendula was used to treat various skin diseases, ranging from skin ulcerations to eczema. Internally, the soothing effects of calendula have been used for stomach ulcers and inflammation.

Other indications include:

- Antiseptic, anti-inflammatory, healing, and soothing.
- Infusion of the petals used as lotion for skin cleansing and softening.
- Taken internally for poor circulation, varicose veins, ulcers, colitis, stomach cramps; also, headaches, toothache, ague, and skin problems.
- Said to strengthen and comfort the heart and aid indigestion.
- For external use, an oil is made from the flowers for skin problems and sunburn; used in ointment form to heal acne and fade old scars and for external sores, cuts, bruises, burns and rashes.
- Usually combined with chamomile and comfrey for a soothing ointment in cases of skin problems, burns, cuts, insect bites, stings and bruises.
- An infusion from the leaves is used for tired swollen feet.
- Flowers used in infusion form as a wash for red eye.

Dosage:

- A tea of calendula can be made by pouring 200 ml of boiling water over 1-2 teaspoons of the flowers, which is steeped, covered for ten to fifteen minutes, strained, and then drunk. At least 3 cups of tea are generally drunk per day.
- Tincture is similarly used three times a day, taking 1-2 ml each time. The tincture can be taken in water or tea.
- Prepared ointments are often useful for skin problems, although wet dressings made by dipping cloth into the tea (after it has cooled) are also effective.
- Juice: Take 1 tsp. At a time, always freshly pressed.
- Tincture: To make, soak a handful of flowers in 0.5 quart rectified alcohol or whiskey for 5 to 6 weeks. A dose is 5 to 20 drops.
- Salve: Boil 1 oz dried flowers or leaves, or 1tsp fresh juice, with 1 oz of lard.

Alternative Names:

Calendula officinalis; Garden marigold; Pot marigold

Other Names: Marigold, garden marigold, holigold, Mary bud, pot marigold, Calendula

CHAMOMILE FLOWER

Figure: 4

Description

Chamomile is a daisy-like flower, a member of the family *Asteraceae* (also called by its older name *Compositae*.) The active compounds in German and Hungarian chamomile are extracted and used in herbal remedies. Other varieties of the plant such as Roman or English Chamomile (*Chamaemelum nobile*), which contain similar compounds, are not used as often for herbal remedies.

Other common name(s): German chamomile, Hungarian chamomile

Scientific/medical name(s): *Matricaria chamomilla, Matricaria recutita,*

Overview:

German chamomile is an herb. People use the flower head of the plant to make medicine.German chamomile is used for intestinal gas,

travel sickness, stuffy nose, hay fever, nervous diarrhea, attention deficit-hyperactivity disorder (ADHD), fibromyalgia, restlessness, and trouble sleeping.

Active constituents

German chamomile promotes relaxation and reduces swelling (inflammation). German chamomile might reduce swelling by slowing the production of prostaglandins, leukotrienes, and histamines.

Medicinal Uses

- Upset stomach (dyspepsia), when a specific product (Iberogast, Medical Futures, Inc) that combines of German chamomile and other herbs is used. The combination includes German chamomile plus peppermint leaf, clown's mustard plant, caraway, licorice, milk thistle, celandine, angelica, and lemon balm.
- Colic in breast-fed infants when used in combination with other herbs. A specific product containing 164 mg of fennel, 97 mg of lemon balm, and 178 mg of German chamomile (ColiMil, Milte Italia SPA) taken twice daily for a week seems to reduce crying in breast-fed infants with colic.
- Treating or preventing swelling and deterioration (mucositis) of the mouth lining caused by radiation therapy and some types of chemotherapy, when used as a mouth rinse.

Side effects

German chamomile can cause allergic reactions in some people. It is in the same plant family as ragweed, marigolds, daisies, and other related herbs.

When applied to the skin, German chamomile can cause allergic skin reactions. When applied near the eyes, German chamomile may cause eye irritation.

Special Precautions & Warnings:

- **Pregnancy and breast-feeding**: Not enough is known about the use of German chamomile during pregnancy and breast-feeding. Stay on the safe side and avoid use.
- **Allergies to ragweed or related plants**: German chamomile may cause an allergic reaction in people who are sensitive to the Asteraceae/Compositae family of plants.
- **Hormone-sensitive condition such as breast cancer, uterine cancer, ovarian cancer, endometriosis, or uterine fibroids**: German chamomile might act like estrogen in the body.

Interactions

- **Birth control pills** (Contraceptive drugs) : Some birth control pills contain estrogen. German chamomile might have some of the same effects as estrogen. But German chamomile isn't as strong as the estrogen in birth control pills.
- **Estrogens** interacts with GERMAN CHAMOMILE : Large amounts of German chamomile might have some of the same

effects as estrogen. But large amounts of German chamomile aren't as strong as estrogen pills.Some estrogen pills include conjugated equine estrogens (Premarin), ethinyl estradiol, estradiol, and others.

- **Medications metabolized by the liver** (Cytochrome P450 1A2 (CYP1A2) substrates) interacts with German chamomile
  - Some medications are broken down by the liver. German chamomile might decrease the metabolism some medications.
  - These include amitriptyline, haloperidol, ondansetron, propranolol, theophylline, verapamil and others.
  - Benzodiazepines also interact with German chamomile. Also other sedatives Pentobarbital, phenobarbital, secobarbital, fentanyl morphine, zolpidem and others.
  - **Tamoxifen** interacts with GERMAN CHAMOMILE

Dosing

By mouth

- For upset stomach: A specific combination product containing German chamomile (Iberogast, Medical Futures, Inc) and several other herbs has been used in a dose of 1 mL three times daily.
- For damage to the inside of the mouth caused by chemotherapy or radiation treatments: A mouth rinse made with 10-15 drops of German chamomile liquid extract in 100 mL warm water three times daily.

ALOE VERA

Figure: 5

The aloe vera -A natural medicine for cancer, cholesterol, diabetes, inflammation, IBS, and other health conditions.

In a single plant, aloe vera offers potent, natural medicine that:

- Halts the growth of cancer tumors.
- Lowers high cholesterol.
- Repairs "sludge blood" and reverses "sticky blood".
- Boosts the oxygenation of your blood.
- Eases inflammation and soothes arthritis pain.
- Protects the body from oxidative stress.

- Prevents kidney stones and protects the body from oxalates in coffee and tea
- Alkalizes the body, helping to balance overly acidic dietary habits
- Cures ulcers, IBS, Crohn's disease and other digestive disorders.
- Reduces high blood pressure naturally.

- Nourishes the body with minerals, vitamins, enzymes and glyconutrients.
- Accelerates healing from physical burns and radiation burns.
- Replaces dozens of first aid products, makes bandages and antibacterial sprays.
- Halts colon cancer, heals the intestines and lubricates the digestive tract.
- Ends constipation.
- Stabilizes blood sugar and reduces triglycerides in diabetics.
- Prevents and treats candida infections.
- Protects the kidneys from disease.
- Functions as nature's own "sports drink" for electrolyte balance
- Boosts cardiovascular performance and physical endurance.
- Speeds recovery from injury or physical exertion.
- Hydrates the skin, accelerates skin repair.

Aloe vera boosts immune function and destroys cancer tumors

Scientific research shows strong immunomodulatory and antitumour properties for aloe vera polysaccharides. That means the gel helps boosts immune system function while destroying cancer tumors. One study published in *International Immunopharmacology* (1995) showed that aloe vera polysaccharides exhibited potent macrophage-activating activities including producing increased volumes of nitric oxide (which has antitumor potential).

Aloe vera halts inflammation

Using aloe topically is well known to ease inflammation of joints, reducing arthritis pain. But aloe can also be used internally, reducing inflammation throughout the body from the inside out. People who drink aloe vera for two weeks typically begin to experience a significant reduction of inflammation symptoms.

Aloe vera enhances skin health

Aloe is one of the most widely-used ingredients in high-grade skin care products. There's a reason for that: It's great medicine for the skin! Aloe soothes the skin, hydrates it, nourishes it and accelerates the regeneration of new skin tissue

Aloe vera stabilizes blood sugar in diabetics

Diabetic patients who take aloe vera for 3 months experience a significant drop in fasting blood sugar levels. They also exhibit lower cholesterol levels and slight improvements in total cholesterol.

Aloe vera lowers cholesterol and triglycerides

When used internally, aloe vera gel improves the quality of the blood and helps rebalance the blood chemistry in a way that lowers cholesterol and total triglycerides (in people with elevated levels).

Aloe vera relieves joint and muscle pain

This effect is directly related to the inflammation factor mentioned above. It works when used both internally and externally. Essentially, aloe reduces overall inflammation.

Aloe vera amplifies the antioxidant effects of vitamins

This is an especially interesting effect of aloe: It makes vitamin C, vitamin E and other antioxidants work better! It actually potentiates antioxidants, probably due to its effect on enhancing blood quality and allowing the blood to more effectively transport oxygen and nutrients to the body's cells

Aloe vera cures ulcers, IBS, Crohn's disease and Celiac disease

Polysaccharides in the aloe vera plant have curative effects on numerous digestive disorders. The Internet is a storehouse of information and testimonials about aloe vera curing IBS, ulcers, Crohn's disease and other disorders of the digestive tract.

Aloe vera contains acemannan, a natural immune booster

There's research being done now on the anti-cancer effects of acemannan, a phytonutrient found in aloe vera. In one study, dogs and cats undergoing radiation for cancer were given acemannan as an adjunctive therapy.

Aloe vera heals radiation burns from radiation cancer treatments

For those cancers treatment victims who have been maimed by radiotherapy treatments, applying aloe vera topically to the radiation area will rapidly accelerate the healing response.

The abstract states:

Radiomodifying effects of the leaf extract of Aloe vera were observed on the testes of Swiss albino mice at 50 and 100 mg/kg dose levels. This extract was non-toxic when injected up to 800 mg/kg, and significant enhancement in survival time of the irradiated group was observed. In addition, treatment reduced radiation-induced damage to germ cells and loss in *body weight*.

Contents of aloe vera gel

- Water
- 20 minerals
- 12 vitamins
- 18 amino acids
- 200 active plant compounds (phytonutrients), including:

    Enzymes

    Triterpenes (a phytonutrient that lowers blood sugar)

    Glyconutrients & glycoproteins

    Polysaccharides, including: Acemannan, mannose-6-phosphate

RUBIA CORDIFOLIA

Figure: 6

Rubia cordifolia, often known as **Common Madder** or **Indian Madder**, is a species of flowering plant in the coffee family, Rubiaceae. It has been cultivated for a red pigment derived from roots.

Common names of this plant include **Manjistha** in Sanskrit, Marathi, Kannada and Bengali, **Majith** in Hindi and Gujarati, **Tamaralli** in Telugu, **Manditti** in Tamil.

Description

- It can grow to 1.5 m in height. The evergreen leaves are 5–10 cm long and 2–3 cm broad, produced in whorls of 4-7 starlike around the central stem. It climbs with tiny hooks at the leaves and stems. The flowers are small (3–5 mm across), with five pale yellow petals, in dense racemes, and appear from June to August, followed by small (4–6 mm diameter) red to black berries.

- The roots can be over 1 m long, up to 12 mm thick. It prefers loamy soils with a constant level of moisture. Madders are used as food plants for the larvae of some Lepidoptera species including Hummingbird hawk moth
- Rubidianin, rubiadin, RA-7, RA-700 and RC-18 isolated from *Rubia cordifolia* inhibit growth & spread in cancers of breast, ovary, cervix, colon, lung, malignant ascites, malignant lymphoma, malignant melanoma sarcoma and leukaemia. Rubiadin also possesses hepatoprotective activity..
- The plant grows throughout India, in hilly districts upto 3500 meters height. It is a perennial, herbaceous climber. The stems are often long, rough and grooved, with woody base. The leaves often in whorls of four. They are 5-10 cm long, variable, cordate – ovate to cordate-lanceolate, rough above and smooth beneath.
- The flowers, 0.3-2.5 cm long, blackish or greenish black, in terminal panicled glabrous cymes. The fruits are globose, fleshy, smooth, purplish black when ripe and shining. The roots are 4-8 cm long, reddish, cylindrical, flexuous, with a thin red bark.
- The botanical name of Manjistha is *Rubia cordifolia* and it belongs to family rubiaceae. The roots contain resinous and extractive matter, gum, sugar, coloring matter, - the salt of the pigment being a red crystalline principle purpurine.
- Other compounds isolated are xantho-purpurin, glucose, sucrose and ruberythric acid. Alizarin, purpurin, purpurin carbohydrate, quinizarine and christofin isolated from roots. Antitumor cyclic hexapeptides – RA-V and RA-VII – isolated from roots.

Properties

Manjistha is bitter, astringent and sweet in taste, pungent in the post digestive effect and has hot potency. It alleviates all the three doshas. It possesses dry and heavy (to digest attributes. It is a potent blood purifier and anti diarrhoeal.

Pharmacologic properties

The following properties were described in various cellular and animal models:

- Anti-inflammatory
- Urolithiasis

Uses

- It is used to treat skin infections,leucoderma
- It helps to gain luster and glow of the skin to treat discoloration.
- Externally, Manjistha is highly recommended in skin diseases associated with **edema and oozing**. The wound and ulcers dressed with Manjistha ghrta heal promptly and get dried up and well cleansed. Especially the chronic non-healing and cozying wounds respond very will.
- In fractures, the external splint of Manjistha, madhuka skin and amalaki leaves are beneficial.
- The root powder works well, with ghee, for the medicament of **acne**. Used externally as a paste by itself or with honey, it heals **inflammation** and gives the skin an even tone and smoothness.

- It is a powerful dye, imparting a reddish tinge to the skin and is used in dying the clothes also. Internally, Manjistha is valuable in a vast range of diseases.
- In diarrhoea, Manjistha works well when combined with lodhra (Symplicos racemosa) skin powder.
- Manjistha is benevolent in gastrointestinal ailments like loss of appetite, dyspepsia and worm infestations, as it is an appetizer, digestant, destroys ama and a vermicide.
- Manjistha kvatha is widely used as a blood purifier. It acts mainly on rasa and rakta srotasas, alleviates the kapha and pitta dosas and eliminates toxins. This ameliorates the vitiation of bhrajaka pitta (pitta from the skin) and imparts better complexion to the skin.
- Manjistha was held in high esteem by ancient sages in the treatment of skin diseases. It is widely used, till today, in various skin disorders like erysipelas, eczema, acne, scabies and allergic manifestations.
- Manjistha helps in controlling the irritation of nerves and pacifies the mind, hence salutary in epilepsy, especially of pitta type. The decoction of manjistha, triphala, daruharidra, guduci, katuka, nimba and vaca is used in gout with benefit.
- The cold infusion of Manjistha improves the menstrual bleeding and relieves the pain in dysmenorrheal. It stimulates and cleanses the uterus, so useful in postnatal ailments. The decoction of Manjistha is useful in oligomenorrhea and amenorrhea.

3. LITERATURE REVIEW

LITERATURE SURVEY

An extensive literature survey was carried out regarding "**Prevention of radiation induced Radiodermatitis and its Management"**. The necessary information collected from various literatures was documented.

The literatures supporting the study were gathered from various sources such as Iowa Drug Information Services [IDIS], software released by the College of Pharmacy, University of Iowa &the division of Drug Information Services [DDIS] containing articles from about 250 medical and related journals in & around the world.

JOURNALS:

The various journals used for references were

- Annals of Pharmacotherapy
- European Journal of Cancer
- Journal of Clinical oncology
- The Journal of Immunology
- Gynecologic Oncology
- Journal of Leukocyte
- Clinical and Translational Oncology
- Clinical Cancer Research
- Radiotherapy and Oncology
- The New England Journal of Medicine
- Supportive Care in Cancer

- Southern Medical Journal
- Cancer
- Cancer Nursing
- Caner Control
- International Journal of Cancer
- Journal of Pharmaceutical Sciences
- International Journal of Clinical Pharmacy and Therapeutics
- International Journal of Radiation Oncology Biology Physics

An extensive search for literature was done on important data bases like:

- Medscape
- The Lancet
- Pubmed
- Medline
- Sciencedirect
- Cancerlit
- Radiation Oncology
- The Cochrane Library
- Pubget
- CINAHL
- DARE
- HealthSTAR
- South-East Asia Database

- **H. C. Goldberg M.D *et al.,*** in **1944** suggested that a number of interesting articles have appeared giving quaint historical lore and scientific application of the **Aloe Vera** leaf for dermatologic purposes. Particular application of the leaf has been recommended in radio dermatitis. The first article published on the use of the Aloe Vera leaf in radio dermatitis was written by C. E. Collins and Creston Collins. Dr. C. E. Collins first became interested in the therapeutic use of the leaves in 1935, his son Dr. Creston Collins having seen the Seminole Indians using the leaf of the plant to treat burns. These physicians then applied the leaf for the treatment of radio dermatitis, with encouraging results. Since then, aloe Vera has become widely used for this purpose.

- **C. C. Lushbaugh M.D *et al.,*** in **1953** has done Experimental acute radio dermatitis following beta irradiation**. V. Histopathological study of the mode of action of therapy with aloe Vera.** Rabbits irradiated locally on the back with 14,000 and 28,000 rep of beta radiation and the area was treated with the whole leaf of Aloe Vera and commercially available ointment made from these leaves. The gross and microscopic morphological changes in the skin resulting from the radiation alone were compared with those in the irradiated skin treated with Aloe. Treatment was found to hasten both the degenerative and reparative phases of the lesion so that complete healing of an ulcer caused by 28,000 rep of beta radiation was accomplished within two months of treatment, while the untreated ulcerations were still not completely healed more than four months after

irradiation. It was concluded that A. Vera contains substances that are stimulatory both to the relayed development and delayed healing of ulcerative radio dermatitis and that because of the growing modern importance of this injury further investigation of the action of aloe Vera should be pursued.

- **Cole *et al.*,** in **1935** reported that in 31 year old white women a case or severe roentgen dermatitis with desquamation over an area 4 by 8 cm of the forehead and extending above the hair line. Within 24 hours after the treatment with fresh **aloe**, the itching and burning had subsided completely. Within 5 weeks with continued treatment, there was **complete regeneration of the skin of the forehead and scalp, new hair growth, complete restoration of sensation and absence of a scar**. After 3 months there was no indication of a relapse and upon exposure to sunburn, the forehead was seen to be pigmenting normally along with other exposed skin surfaces . In 1937, Lovemen reported two cases of 40 year old man suffering from severe roentgen ray ulcers on the back of both hands. Treatment with fresh aloe leaf reduced ulceration area 50% within a week and completes healing within a few months.

- **Davis *et al.*,** in **1992** Aloe Vera is a complex plant containing many biologically active substances. Evidence has shown that **Aloe** is effective in wound healing and inflammation reduction .This is attributed to a growth factor-like substance in Aloe which activates the wound healing and inflammation reduction

process.Mannose-6-phosphate and glucose-6-phosphate are the main constituents of the polysaccharide chain in Aloe. Our experiments have shown that mannose-6-phosphate demonstrates wound healing and anti-inflammatory activity in a dose response fashion. Furthermore we concluded that glucose-6-phosphate does not improve wound healing or reduce inflammation. Therefore, our evidence suggests that mannose-6-phosphate is a major structural constituent that stimulates wound healing and anti-inflammation. In summation, we are convinced that M-6-P in aloe directly or indirectly stimulates fibroblast activation. Therefore, it is clear that M-6-P is an important factor in the wound healing process and plays a significant role in the biological activity of Aloe Vera.

- **Robert H. Davis *et al.*,** in **1988** demonstrated in Aloe Vera-A Natural Approach for Treating Wounds, Edema, and Pain in Diabetes. The Diabetic patient suffers from wounds, edema and pain. There was a diminished wound healing mechanism, insensitivity to pain perception, and altered fluid dynamics, resulting in a prolonged edema response. This study dealt with **Aloe Vera (decolorized)** as a mode of treatment to alleviate some of the consequences associated with diabetes. The results in each area tested were favorable. As an aid in promoting diabetic wound healing, tested groups treated with Aloe Vera displayed nearly a 100% increase in wound size reduction as compared to their untreated counterparts. In the area of analgesia, diabetic mice receiving Aloe Vera were able to tolerate a painful stimulus

a full 3 second longer than suitable controls without the total obliteration of responsiveness to stimuli. Additionally, physiologically normal mice treated with Aloe represented nearly 3 times the tolerance to painful stimuli as compared to untreated animals. As an Antiedemic agent, Aloe treated animals experience a five-fold reduction in the edema response as compared to untreated diabetic groups. Aloe Vera has been proven to be an effective agent in the treatment of wounds edema and pain associated with diabetes.

- **Carroll. S .Wright M.D** ***et al.,*** in **1936** has reported that Aloe Vera is used in the treatment of Roentgen ulcers and Telangiectasis. From the case reported, it would seem that x-ray ulceration, even of several years' duration, will respond to the use of Aloe Vera. The permanence of results can be determined only by watching cases thus treated over a period of time. Little can be expected in the treatment of Telangiectasis as a result of irradiation beyond a smoothing and softening of the affected skin. The use of the **fresh whole leaf of Aloe Vera** in the treatment of Roentgen dermatitis was suggested by C. E. and Creston Collins. Early in 1935, they reported a case of a woman, aged 31, who had a severe Roentgen dermatitis of the left forehead following a depilating roentgen treatment. Various local treatments were tried without effect, and exfoliation and severe itching persisted at the treatment site. The patient received a local application of the fresh whole leaf of Aloe Vera to allay the itching. Within 24 hours the sensation of itching and

burning subsided and the condition progressively improved within the next 5 weeks and showed "complete regeneration of skin of the forehead and scalp, new hair growth, complete restoration of sensation, and absence of scars.

- **Zawahry M.** ***et al.*****,** in **1973** reported the use of Aloe in treating leg ulcers and dermatoses. His report deals with Aloe's use locally in chronic leg ulcers, seborrhea, acne vulgaris, alopecia (hair fall), and alopecia areata. Drawings of the plant found on the walls of ancient Egyptian temples show that its pulp was used externally for treatment of burns, ulcers and parasitic infections of the skin**. Aloe Vera** has been used with some success in the treatment of various dermatological conditions, radiation ulcers, internal diseases such as peptic ulcers and burns. Aloe Vera proved to have a stimulating effect on the rate of healing of chronic leg ulcers. They believe improvement in three patients treated can be attributed to improvement in the peripheral circulation which is deficient in such patients. The drug appears to stimulate hair growth and drying of seborrheic skin. Improvement was noted after treatment of patients with seborrheic alopecia, acne vulgaris and alopecia areata.

- **World Health Organization** in **1999** published Monographs on selected medicinal plants, including Aloe Vera which states that aloe Vera Gel is widely used for the external treatment of minor wounds and inflammatory skin disorders. The gel is used in the

treatment of minor skin irritations, including burns, bruises, and abrasions. Aloe Vera has been effectively used in the treatment of first and second degree thermal burns and radiation burns. Both thermal burns and radiation burns healed faster with less necrosis when treated with preparations containing **Aloe Vera Gel**. Healing of radiation ulcers was observed in two patients treated with Aloe Vera cream. Complete healing was observed, after treatment with fresh Aloe Vera Gel, in two patients with radiation burns. Twenty-seven patients with partial thickness burns were treated with Aloe Vera Gel in a placebo-controlled study. The Aloe Vera Gel-treated lesions healed faster (11.8 days) than the burns treated with petroleum jelly gauze (18.2 days), a difference that is statistically significant (t-test, $P < 0.002$).

- **W. R. Sage, Inc *et al.*,** in **1977** reported that in both medical and cosmetic practices, the Aloe Vera plant was used consistently through the centuries for such varied conditions as wounds, stomach disorders, headaches, gum and mouth disease, constipation, hemorrhoids, kidney problems, insomnia, pruritis, burns, **dermatitis**, herpes, fungal infections, loss of hair, indigestion, insect stings, dysentery, prostatitis, colds and body odors. Some of the earliest scientific research was performed in 1935 by researchers for the Atomic Energy Commission. They concluded that Aloe Vera was the most effective product known for the treatment of radiation burns of the skin.

- **In 2004** Anatomy of an ingredient: Aloe Vera published by The Independent, London THE ALOE plant consists of around 400 different species, and was first originated in Africa. The type of Aloe grown commercially in America (North and South), Asia, Africa, Australasia and southern Europe, is the Aloe Barbadensis Miller plant, known as aloe Vera - Latin for "true aloe". This exceptional plant contains a wide range of amino-acids, enzymes, minerals, vitamins and other micronutrients. The sap of the aloe contains substances called anthraquinones that have antibacterial, antiviral, antifungal, anti-inflammatory, analgesic and anaesthetic properties. It boosts the immune system, provides antioxidant vitamins A, C and E, helps healing, lubricates joints, and is an effective tonic. Aloe Vera can be used on the skin, to treat rashes, sunburn, **dermatitis,** eczema and psoriasis. It can also be taken internally, and is useful for conditions like colitis, arthritis, IBS, asthma, and chronic fatigue. Opt for Aloe Vera products that are listed as 98-99 per cent pure, as these will be higher in the protective mucopolysaccharides that have a healing effect on the gut.

- **Srinivas, C.R.** ***et al.,*** in **2003** aggravated the pre-existing dermatosis with Aloe Vera. A 65-year-old man presented with recurrent generalized itching since 1 year. Examination revealed lichenified skin over the face and extensors of both extremities. He gave a history of rubbing the pulp of Aloe Vera leaves on to his lesions whenever his itching worsened. Clinically, we suspected allergic contact dermatitis, possibly aggravated with

Aloe Vera. He was patch tested with the plant series by CODFI, which included parthenium 0.5%, xanthium 0.5%, chrysanthemum 0.5%, control and pulp of Aloe Vera, and the results were interpreted as recommended by ICDRG. He tested positive to Aloe Vera on day 2 and day 3. One of the authors (CRS) tested negative to the pulp, thus ruling out irritant dermatitis. Allergic contact dermatitis to Aloe Vera has been reported earlier. The gelatinous material inside the leaf of Aloe Vera has been recommended from ancient times for the alleviation of inflammatory changes in the skin. More recently it has been advocated in the **treatment of radio dermatitis and** leg ulcers. It is a common ingredient in numerous topical moisturizers (e.g. Elovera, Sofderm, and Dewderm). Aloe consists of a variable mixture of aloin, aloemodin and other substances. Aloin is an anthraquinone that may be regarded as a potential sensitizer. This report highlights the fact that even commonly used; relatively safe medications can occasionally cause sensitivity.

- **Momoe Soeda *et al.,*** in **1964** has done studies on the effect of Cape Aloe for irradiation leucopenia. Studies on the prophylactic and therapeutic effects on leucopenia caused by exposure to Cobalt-60, and studies on protective and therapeutic effect of Marinamycin against leucopenia in X-ray irradiated rabbits were reported by SOEDA and Solcoseryl was also used for evaluation. In the course of studies and prophylactic and therapeutic effects of aloelin and aloe-B fraction on leucopenia induced by **Cobalt-**

60 irradiation, some impressive findings were derived there from, the reports of which is herein described. Therapeutic intravenous and subcutaneous administration of aloelin and aloe B fractions five or seven consecutive days in dosage ranging 100 mcg rabbit subsequent to the whole body irradiation of Cobalt resulting in improving the WBC counts.

- **Smoot, E. Clyde (MD)** ***et al.,*** in **1981** deals with the effects of anti-inflammatory agents on acute and late radiation skin changes in the rat. This article by the **University of Chicago Burn Center** deals with one of the earliest recognized benefits of **Aloe Vera**. Back in the thirties, when x-Ray treatments were first being used, medical reports showed that Aloe Vera was the only thing that would heal many of the radiation induced lesions of the skin. Now, with this testing on rats, the data is established in true, scientific testing. The purpose of the study is to examine pharmacological methods of altering acute and late skin changes secondary to irradiation and to evaluate the role of prostaglandins and thromboxane as mediators of acute and late radiation skin pathology. Acute radiation changes in human skin include endothelial swelling and proliferation with thrombosis of larger dermal vessels. He has noted the limitation of progressive dermal ischemia after thermal injury to the skin of guinea pigs by inhibiting the local accumulation of thromboxane in radiation pathology. Vascular occlusive changes with resulting skin ischemia precede later changes of increased collagen deposition. Attenuation of the acute inflammatory

changes of radiation exposure may be expected to decrease chronic ischemic changes in the skin.

- **Murray, Frank *et al.*,** in **1994** demonstrated the Therapy and treatment with Aloe Vera. Researchers around the world, Texas, Japan, Israel are hard at work analyzing the many medicinal properties of the approximately 600 varieties of Aloe plants, which are being used successfully to treat burns, X-ray and **radiation dermatitis,** gastric ulcers, sunburn, frostbite, GI disorders, constipation, diabetes, etc., It penetrates injured tissue, relieves pain, is Anti-inflammatory and dilates capillaries, thereby increasing the blood supply to the injured area. They found that partial thickness burn wounds treated with Aloe extracts healed faster and had les tissue loss than patients treated with standard techniques. The researchers explained that Aloe inhibits a devastating vasoconstrictor known as TxA2 and keeps it from being produced, while maintaining a balance between several prostaglandins, the powerful hormones that impact on pain, healing etc**., Aloe juices and gels** have been shown to have antibacterial and antifungal properties and they appear to be active against a broad spectrum of microbes. Salicylate, which have both anti inflammatory and pain killing characteristics are found in Aloe also Magnesium lactate, a substance which can inhibit histamine reactions like itching and irritation, and enzymes of bradykinin inhibitor are presented. Bradykinin produces pain in inflamed tissue.

- **Mandeville, Frederick B. (MD)** ***et al.,*** in **1939** has done the study on Aloe Vera in the treatment of radiation ulcers of mucous membranes. It is reported that the jelly is placed in contact with the floor of the ulcer and held in place with the bandage. Dressings are changed once or twice daily. The treatment seems to be effective in indolent roentgen and radium ulcers. Often the pain disappears within a day or two and healing takes place in a few weeks or a few months. Good results have been obtained also in ulcers that occurred early in third-degree ulcers. A 54 year old male had noticed a growth 1 cm in diameter on the right side of his tongue and floor of his mouth anteriorly for three months. This was removed by a surgeon with electrocautery and the pathologist diagnosed as squamous cell epithelioma grade 3. Intra oral radium therapy heavily filtered and external deep x-ray therapy was administered over a ten day period. The ulcer was deep and measured 5x1.5 cm. **Aloe Vera gel** was applied by the patients. Relief from pain was prompt and definite and the ulcer slowly grew smaller, after another five weeks the ulcer was completely healed. They concluded that Radiation ulcers of the mucous membranes and adjacent tissues of body cavities may also be treated with the fresh leaf of Aloe Vera.
- **Loveman, Adolph B. (MD)** ***et al.,*** in **1937** reported that Aloe Vera in used in the treatment of Roentgen ray ulcers. He has reported that two cases of roentgen ray ulcers are reported in which complete healing followed the use of the **fresh whole leaf of Aloe Vera**. The duration of the ulcer is important with regard to immediate prognosis. In the two cases under consideration

pain disappeared and healing occurred much sooner in the ulcer which had been present the shorter period of time. It is felt that treatment should be continued with the fresh whole leaf for atleast from three to nine months before the condition is considered refractory or the treatment is discontinued. In the two cases reported the fresh whole leaf of Aloe Vera proved to be much more efficacious than the ointments including bismuth subnitrate and neoarsphenamine in the treatment of the ulcer. The latter, however, was fairly satisfactory in treating some of the smaller keratoses and in improving the general tone and texture of the skin. In both cases there were marked increase in pain and definite progression in the size of the ulcerations while pavaex treatment was used.

- **Skousen, Max B *et al.*,** in **1982** published in his Hand Book, The Ancient Egyptian Medicine Plant that Aloe Vera has about one and half million species and one-fourth of the two billion prescriptions filled in the United States contain botanical derivatives such as alkaloids, Glycosides, Steroids etc., In the first century it is reported that **Aloe Vera** has been effectively used to treat burns, healing wounds, insomnia, constipation, GI disorders. Los of hair gum and mouth disorders blistering, sun burn, blemishes, ulcerated skin lesions, eczema and relieving aches and pains and it reduces the itching and scaling and greatly improving the skin appearance. The recent history reveals that Aloe Vera is highly effective in skin ulcerations caused by radiation burns. It is also reported that Aloe Vera is

used for cuts and wounds, digestive problems, hair and scalp care, hemorrhoids and bleeding piles, infections, poison ivy, poison oak, allergies, psoriasis and eczematous rashes, scar removal, stretch marks from pregnancy, varicose veins, skin cancer, scrapes and abrasions, stings by insects, jellyfish, stinging nettle, etc., ulcers, arthritis, brown skin spots, acne, animal first-aid, sinus, general health maintenance, asthma, sore throat, eye and ear drops.

- **Danhof, Ivan E. (PhD, MD)** ***et al.,*** in **2002** demonstrated in his book Internal uses of Aloe Vera; the anti-cancer activity was explained that one of the common experimental cancer models is sarcoma-180. When Aloe was administered to mice bearing S-180 tumors, the tumor growth was inhibited. Similarly**, Alexin B,** a species derived from Aloe, was shown to possess **anti-cancer activity** against lymphocytic leukemia. Additional investigations revealed that another molecular species derived from Aloe, Aloctin-A, had **anti-tumor activity,** but the action was to bolster the immune system rather than a direct anti-tumor activity.

- **Richardson J et al., in 2005 h**as done a study to systematically review and critically appraise the evidence for effectiveness of **Aloe vera gel** for radiation-induced skin reactions. Major biomedical databases and specialist complementary and alternative medicine databases were searched. Relevant research was systematically categorised by study type and

appraised according to study design. He concluded that there is no evidence from clinical trials to suggest that topical Aloe vera is effective in preventing or minimising radiation-induced skin reactions in cancer patients. Further methodologically rigorous research studies should be conducted to evaluate the effectiveness of currently used and novel therapies for the prevention, minimisation and management of radiation-induced skin reactions.

- **Mihkaila Maurine et al.,** in **2004** has done a study to review historical and current research data on prevention and treatment of **acute radiation dermatitis**. His data synthesis reveals that Washing the skin with mild soap and water and the hair with mild shampoo is safe during radiation therapy. Biafine (Medix Pharmaceuticals, Inc., Largo, FL), almond ointment, topical vitamin C, and gentian violet have not been proven effective and should not be used. Aloe vera is beneficial and also they are not harmful. He concluded that Nurse clinicians and nurse scientists must partner to conduct further research about the prevention and management of acute radiation dermatitis and develop comprehensive evidence-based clinical practice guidelines.

- **Sue Heggie et al** in **2002** has done a Phase III study on the efficacy of topical aloe vera gel on irradiated breast tissue. The aim of the study was to see if topical **aloe vera gel** would be

beneficial in reducing the identified skin side-effects of radiation therapy, including erythema, pain, itching, dry desquamation, and moist desquamation, when compared with aqueous cream. Patients were randomized to either topical aloe vera gel or topical aqueous cream to be applied 3 times per day throughout and for 2 weeks after completion of radiation treatment. Weekly skin assessments were performed by nursing staff. Aloe vera gel did not significantly reduce radiation induced skin side effects. Aqueous cream was useful in reducing dry desquamation and pain related to radiation therapy.

- **Olsen DL et al.,** in **2001** has done a study on the effect of aloe vera gel/mild soap versus mild soap alone in preventing skin reactions in patients undergoing radiation therapy. The purpose of the study was to determine whether the use of mild soap and **aloe vera gel** versus mild soap alone would decrease the incidence of skin reactions in patients undergoing radiation therapy. The mean age of the participants was 56 years. The group consisted of Caucasians (74%) and African Americans (26%). The ethnic mix was non-Hispanic (65%) and Hispanic (35%).His findings was at low cumulative dose levels < or = 2,700 c Gy, no difference existed in the effect of adding aloe. When the cumulative dose was high (> 2,700 c Gy), the median time was five weeks prior to any skin changes in the aloe/soap arm versus three weeks in the soap only arm. When the

cumulative dose increases over time, there seems to be a protective effect of adding aloe to the soap regimen.

- **M S Williams et al.,** in 1996 has done a Phase III double-blind evaluation of an aloe vera gel as a prophylactic agent for **radiation-induced skin toxicity.** The purpose of the study was Considerable pilot data and clinical experience suggested that an aloe vera gel might help to prevent radiation therapy-induced dermatitis. Two Phase III randomized trials were conducted. The first one was double blinded, utilized a placebo gel, and involved 194 women receiving breast or chest wall irradiation. The second trial randomized 108 such patients to aloe vera gel vs. no treatment. Skin dermatitis was scored weekly during both trials both by patients and by health care providers. The results revealed that Skin dermatitis scores were virtually identical on both treatment arms during both of the trials. The only toxicity from the gel was rare contact dermatitis. So he concluded that this dose and schedule of an aloe vera gel does not protect against radiation therapy-induced dermatitis.

- **Maurene McQuestion Semin et al**., in **2011**has given Evidence-based skin care management in radiation therapy: clinical update. The purpose of the study was to present a clinical update on the available evidence for the prevention and management of radiation skin reactions (radio dermatitis). There continues to be insufficient evidence in the literature to

recommend a variety of topical or oral agents in the prevention of skin reactions. Radiation treatment techniques are the most promising intervention in reducing the degree of skin reaction. The use of **calendula cream** may reduce the incidence of grade 2 or 3 reactions in women with breast cancer. Oncology nurses need to be aware of the evidence and lack of evidence when recommending interventions to their patients and avoid undue marketing influence when suggesting interventions for the management of skin reactions. Further research is required to evaluate specific interventions in both the prevention and management of radiation dermatitis.

- **Benomar S et al.,** in **2010** has done a study on Treatment and prevention of acute radiation dermatitis. He observed that **acute radiation dermatitis** is a common side-effect of radiotherapy which often necessitates interruption of the therapy. Currently, there is no general consensus about its prevention or about the treatment of choice. The goal of this work was to focus on optimal methods to prevent and manage acute skin reactions related to radiation therapy and to determine if there are specific topical or oral agents for the prevention of this acute skin reaction. The prevention and the early treatment are the two focus points of the management of the acute radiation dermatitis.

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- **Maurene McQuestion Semin et al.,** in **2006** has given Evidence-based skin care management in radiation therapy.

The objective of the study was to review published studies evaluating interventions for the prevention and management of radiation skin reactions/dermatitis. He concluded that there is insufficient evidence in the literature to recommend specific topical or oral agents in the prevention or management of skin reactions. Recent limited evidence suggests that the **use of calendula cream** may reduce the incidence of grade 2 and 3 reactions in women with breast cancer. Additionally, early studies evaluating the use of barrier films or creams may improve moist desquamation.

- **Amanda Bolderston et al.,**in **2006** has given The prevention and management of acute skin reactions related to radiation therapy: a systematic review and practice guideline. The goal of the work is to find the optimal methods to prevent acute skin reactions (occurring within the first 6 months of irradiation) related to radiation therapy and its management. Cancer Care Ontario's **Supportive Care Guidelines Group (SCGG)** conducted a systematic review of literature. Twenty-eight trials meeting the inclusion criteria were identified. Of the twenty-three trials that evaluated preventative methods, Some evidence suggested topical steroid creams and calendula ointment might be effective.

- **Pommier P et al.,** in **2004** has done a Phase III randomized trial of Calendula officinalis compared with trolamine for the prevention of acute dermatitis during irradiation for breast

cancer. The goal of this study was to compare the **effectiveness of calendula** (Pommade au Calendula par Digestion; Boiron Ltd, Levallois-Perret, France) with that of trolamine (Biafine; Genmedix Ltd, France), which is considered in many institutions to be the reference topical agent.He concluded from the study that Calendula is highly effective for the prevention of acute dermatitis of grade 2 or higher and should be proposed for patients undergoing postoperative irradiation for breast cancer

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- **Clavère P et al.,** in **2008** has proposed Radiation induced skin reactions which stated that Radiotherapy is one of the most important treatment modality of cancers. **Skin secondary effects** are well known. Cutaneous complications are described. Physiopathogenic mechanisms are reported. Many preventative and treatment options have been used with varying degrees of evidence of success. Information of patients, further research studies and a multidisciplinary approach are necessary to increase the management of radiation induced skin reactions.

- **Maenthaisong R et al.,** in **200**1 has given the efficacy of aloe vera used for burn wound healing: a systematic review. Aloe vera has been traditionally used for burn healing, The purpose of the study was to conduct a systematic review to determine the efficacy of topical aloe vera for the treatment of burn wounds. Only controlled **clinical trials for burn healing** were

included. Four studies with a total of 371 patients were included in this review. Based on a meta-analysis using duration of wound healing as an outcome measure, the summary weighted mean difference in healing time of the aloe vera group was 8.79 days shorter than those in the control group (P=0.006). Cumulative evidence tends to support that aloe vera might be an effective interventions used in burn wound healing for first to second degree burns.

- **Feily A et al.,** in **2009** Aloe vera in dermatology: a brief review. Aloe vera Linne or aloe barbadensis Miller is a succulent from the Aloe family (400 different species), a tropical plant which is easily grown in hot and dry climates and widely distributed in Asia, Africa and other tropical areas. The aim of this systematic review was to summarize all dermatology-oriented in vitro and in vivo experiments and clinical trials on aloe vera preparations. Extensive literature search were carried out to identify all in vitro and in vivo studies as well as clinical trials on the subject. Forty studies were located. The results suggest that oral administration of aloe vera in mice is effective on wound healing, can decrease the number and size of papillomas and reduce the incidence of tumors and leishmania parasitemia by >90% in the liver, spleen, and bone marrow. . It can also be used as a biological vehicle and an anti-microbial and antifungal agent and also as a candidate for photodynamic therapy of some kinds of cancer.

- **Hosseinimehr SJ et al**., in **2010** has given the Effect of **aloe cream** versus sulfadiazine for healing burn wounds in rats. The aim of the study was to evaluate the efficacy of aloe vera cream in the treatment of thermal burn wounds and to compare these results with silver sulfadiazine in rats. Animals were divided into 4 groups and administered topical cream at 24hr of burn injury induced by hot water. On 25th day wound size was significantly smaller in aloe group as compared with other groups. The result of the study showed aloe cream to significantly increase re-epithelialization in burn wounds as compared with silver sulfadiazine.

- **Reuter J et al.,** in **2008** has done the study of Investigation of the Anti-Inflammatory Potential of **Aloe vera Gel (97.5%)** in the Ultraviolet Erythema Test. 40 volunteers with skin type II and III were included in the randomized, double-blind, placebo controlled, phase III monocenter study. The result was aloe vera gel(97.5%)significantly reduced UV-induced erythema after 48h,being superior to 1% hydrocortisone in cream was more efficient than aloe vera gel. He concluded that aloe vera gel tested might be useful in the topical treatment of inflammatory skin conditions such as UV-induced erythema.

- **Khorasani G et al.,** in **2009** conducted this clinical study, Aloe versus silver sulfadiazine creams **for second-degree burns**: a randomized controlled study to evaluate the efficacy of aloe

vera ream for partial thickness burn wounds and compare its results with those of silver sulfadiazine. 39 patients with II degree burns at two sites on different parts of the body were included in this study where one side treated with SSD and other with aloe cream. The result clearly demonstrated the greater efficacy of aloe cream over SSD cream for treating second degree burns.

- **Srivastava JK et al.,** in **2009** has done the study of Chamomile, a novel and selective COX-2 inhibitor with anti-inflammatory activity. Inducible cyclooxygemase (cox-2) has been implicated in the process of imflammation and carcinogenesis. **Chamomile** has long been used in traditional medicine for the treatment of inflammatory diseases. The aim of the study was to investigate whether chamomile interferes with the COX-2 pathways. The data suggest that chamomile works by a mechanism of action similar to that attributed to non-steroidal anti-inflammatory drugs.

- **Hamman JH et al.,** in **1998** mentioned that many of the health benefits associated with Aloe vera have been attributed to the polysaccharides contained in the gel of the leaves. These biological activities include promotion of wound healing, antifungal activity, hypoglycemic or antidiabetic effects anti-inflammatory, **anticancer,** immunomodulatory and gastroprotetive properties. While the known biological

activities of aloe vera will be briefly discussed. It is the aim of this review to further highlight recently discovered effects and applications of the leaf gel. These effects include the potential of whole leaf or inner fillet gel liquid preparations of aloe vera to enhance the intestinal absorption and bioavailability of co-administered compounds as well as enhancement of skin permeation.

- **Crewe, J.E. (MD)** ***et al.,*** in **1937** experimentally proved in his work "The External uses of Aloe Vera" that the fresh leaves of **Aloe Vera** have many properties which includes, they relieve pain, itching and burning, they have some sort of antiseptic action, infected lesions quickly become clean and exude little or no pus, they seem to stimulate rapid granulation and formation of new tissue so that denuded areas appear to heal more rapidly than with other agents. They are effective in eliminating the foul odors that accompany infection of broken down carcinomas, ulcers and so forth. A single individual after amputation on the stumps of the legs with several ulcers and the condition of developed lymphedema was treated with the Aloe leaves. The circulation in the stumps was poor and several large ulcers had developed. They had shown no inclination to heal under various kinds of treatment. The ulcers were deep and measured to be 5by 13cm and 3cm in diameter. Within twenty-four hours after application of the leaf of Aloe Vera, pain had practically disappeared and the edema was much reduced. The smaller ulcers healed in about two weeks, leaving practically no scar. The large ulcers also made good progress.

- **Castillo, Rafael (MD). (N.D.) et al** in **1968** revealed in his work "Aloe Vera in treating cancer" that he came across several literature and commentaries from cancer specialists on the potential **anti cancer effects of Aloe Vera.** The potential for natural cancer therapy with supplements like aloe Vera and melatonin has been suggested and these substances, called immunomodulants, may benefit certain forms of cancer. A health history of 100 cancer patients who use aloe Vera therapy as a part of their cancer treatment was reviewed, it is found that they receive gluconutrients and experience a reduction in size of squamous cell carcinomas (lung) and oat cell carcinomas (usually originate in the bronchi or lungs). The normal cells appeared protected and abnormal cells appeared more sensitive to treatment when aloe vera was made part of an integrated approach.

- **Robert H.Davis et al.,** in **1987** concluded in his study Aloe vera and wound healing that Wound healing and inflammation in patients present a major problem for podiatrists in the treatment of foot condition. Pressure on skin from tight shoes causes ulcers that heal with difficulty. Heavy steroids and strong synthetic drugs provide major drawbacks because they inhibit wound healing and increase the spread of infection. The present data clearly indicate that Aloe in small doses improves circulation and wound healing. The decolorized **Aloe vera** (without anthraquinones) was more active than the colorized powder. Because of these results, the authors recommend Aloe vera for the wounds.

- **Vogler BK** et al in **1999** conducted a systematic review of its clinical effectiveness. The aim of the study is to define the clinical effectiveness of aloe vera. The use of aloe vera is being promoted for a large variety of conditions. Four independent literature searchers were conducted in **MEDLINE, EMBASE, BIOSIS, and the Cochrane Library.** Only controlled clinical trials were included. Ten studies were located, they revealed that topical application of aloe vera is not an effective preventative for radiation- induced injuries. Even though there are some promising results, clinical effectiveness of oral or topical aloe vera is not suffiently defined at present.

4. SCOPE OF THE STUDY

The scope of the present study is that cancer is one of the leading causes for death among population. Radiotherapy (RT) is used in a wide variety of pelvic malignancies. Radiotherapy alone or combined with cytotoxic therapy and/or surgery is also regarded as standard treatment at a number of primary tumor sites in the various parts of the body.

Although the benefits of this treatment have been well established, a number of patients experience distressing complications due to radiation injury.

Many of the patients undergoing radiation therapy have the complaint of skin toxicity complications.

This may include acute symptoms such as Erythema, Epilation, Desquamation, Edema, Pain, Pigmentation changes etc occurs and in chronic the conditions such as Telangiectasia, ulceration occur.

In some cases, these symptoms resolve after the cessation of radiation but many patients develop chronic illness causing adverse effects that leads to discomfort and decrease the benefits of radiotherapy treatment.

The herbal cream which is composed of four main therapeutically highly valuable drugs has been found to be useful and much safer than other creams in the prevention of skin toxicity complications caused due to radiation therapy.

Amrad cream has the following features:

- Aloe vera in AMRAD Cream increases re-epithelization of wounds enhances skin permeation and demonstrates greater efficacy over other creams.
- Calendula in AMRAD Cream decreases Grade 2 or higher Radiation Dermatitis and reduces the incidence of treatment breaks.
- Chamomile in AMRAD Cream is a novel and selective COX-2 inhibitor with anti-inflammatory and anti-neoplastic effect.
- Rubia cordifolia in AMRAD Cream promotes the healing of the skin tissues and aids in gaining luster and glow of the skin.

Hence apart from the several approaches to decrease the skin complications, this study promises to be the evidence in preventing skin complications in radiation injured cases by applying the Amrad cream.

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5. AIM AND OBJECTIVES

AIM

The aim of the study is to investigate the efficacy of the herbal cream AMRAD in the management of radio dermatitis in Cancer patients.

OBJECTIVES

- To assess the efficacy of Amrad cream in decreasing the incidence and severity of the skin toxicities.
- To measure the skin toxicities by grading according to the skin toxicity assessment tools-radiation therapy oncology group (RTOG) and National cancer institute (NCI).
- To monitor any adverse drug reaction.
- To provide effective counseling to the cancer patients.

6. PLAN OF THE WORK

The entire study was planned to be carried out for a period of nine months from June 2011 – Feb 2012. The proposal was designed as given below.

June'11 – July'11:

- ✓ Obtaining consent from the hospital authorities
- ✓ Literature survey
- ✓ Study design including study design of data entry format (Proforma)
- ✓ Obtaining approval from Institutional Ethics Committee (IEC)

Aug'11 – Dec'11:

- ✓ Selection of patients
- ✓ Obtaining consent from patients
- ✓ Collection of patient details
- ✓ Collection of Lab reports
- ✓ Data Collection

Jan'11 – Feb'12:

- ✓ Data compilation
- ✓ Statistical analysis
- ✓ Data correlation
- ✓ Submission of report

7. METHODOLOGY

STUDY TYPE : Intentional and Retrospective.

CASUALTY ASSESSMENT : RTOG - radiation therapy Oncology Group

NCI – National cancer institute

SAMPLE SIZE : 60 patients with AMRAD

60 patients with control

Totally 120 patients

Patient selection :

- **Inclusion criteria**
- **Exclusion criteria**

Collection of Data :

- **Proforma 1** - Informed Consent Form
- **Proforma 2** - Patient details
- **Proforma 3** - Radiation therapy details
- **Proforma 4** - Investigational parameters
- **Proforma 5** - RTOG Radiation Morbidity Scoring
- **Proforma 6** - Adverse Events report form
- **Proforma 7** - Patient education form

SITE OF THE STUDY

The study on "The Clinical comparison of the Efficacy of a herbal cream for the management of radio dermatitis in Cancer patients" was carried out in the Institute of Oncology in Kavery Medical Centre and Hospital located at Tiruchirappalli, from June 2011 to Feb 2012.

DEPARTMENTS SELECTED FOR STUDY IN THE HOSPITAL:

Patients selected for the study were both inpatients and outpatients from the Oncology Institute of the KMC hospital by getting consent from the Hospital Authority.

CONSENT FORM THE HOSPITAL AUTHORITY

It is customary that every project work carried out in the hospital by the Department of Pharmacy Practice is informed to all the Physicians, Surgeons and other Healthcare Professionals of the hospitals after the approval from Ethics Committee. Henceforth, a protocol of the study, which includes the objectives, methodology, etc., was submitted to the Managing Director of the hospital.

The scholar was permitted to utilize the hospital facilities to make a follow up prescription, in the selected departments. All the health care professionals were well informed through the official circulars and patients were selected as per selection criteria and their consents were taken.

STUDY DESIGN

Design of Data Entry Format [Proforma]

A separate data entry format [Proforma] for incorporating patient details was designed. The format contains details such as Name, Age, diagnosis, Past Medical History etc., The same is given in the appendix.

Proforma- I:

Patient Informed Consent Form.

Proforma- II:

Patient details - Name, Age, Sex, Address, Occupation, Social history, Diagnosis, Past medical history, Tumor differentiation.

Proforma- III:

Radiotherapy details - Name of the patient, Treatment mode and site, Total targeted dose, Daily tumor dose, No of fractions, Treatment duration.

Proforma- IV:

Investigational parameters - This includes the parameters and grading of skin complications according to the Radiation Therapy Oncology Group (RTOG) scale.

Proforma -V:

WHO Skin assessment scale - This includes the scoring and toxicity grading for the assessment of skin complications.

Proforma -VI:

Adverse events assessment

Proforma - VII:

Patient education form - This includes 22 questionnaires that will be asked to the patient on their initial visit and during their radiotherapy treatment. Patient awareness will be created by means of a better patient education.

TYPE OF RADIATION:

External radiation of tele - cobalt60.

DOSE USED:

5000 – 6600 centigray 5 – 6 weeks at 5fractions per week.

PATIENT SELECTION:

INCLUSION CRITERIA:

- Subjects with histologic proof of Cervix, Breast, Head and neck, Lung and Pelvic malignances.
- Be eligible to receive radiotherapy for atleast 5 Weeks duration.
- Both genders
- Age between 30 to 70 years

EXCLUSION CRITERIA:

- Pregnant or lactating women
- Concurrent Use of Immunosuppressant
- Active Infections Including Bacteria, Viral etc…
- Patients with skin allergies/sensitized skin
- Patients with other co-morbities like
    - Inflammatory bowel disease
    - Nephrotic diseases
    - Hepatic diseases
    - Hematopoietic diseases etc**…**

Project work methodology:

1. 120 Patients were selected based on the inclusion - exclusion criteria in the Oncology department of the hospital.
2. All the patients received 2 Gy/ fraction daily, for 5 weeks or more.

3. 60 Patients were treated with Amrad a herbal cream (Group A) to be applied in the morning and night time. They were asked to answer the questionnaire for evaluating the complications.
4. 60 patients were treated as control Group (Group B) without the cream.
5. The following parameters were measured:
    - The grading of complications of redness, hardness, dry desquamation, moist desquamation and atrophy of the skin has been evaluated from 1st week- 6th week by the scale **RTOG (Radiation Therapy Oncology Group) in 1995].**
    - The onset, severity and grading has been done daily for every fractions by the standard scale.
6. Adverse events for both Group A and Group B patients were monitored during the study by using standard Proforma.
7. Patient counseling was done at the entry of the study and at the end of the study.
8. The whole procedure was carried out in cancer patients who were receiving radiotherapy treatment without any alteration therapy.

Procedural details:

The drug for this study (Amrad cream) was given to the patient free of charge by us.

- This study was designed to find out the efficacy of Amrad Cream in prevention of radiation induced skin complications in radiation injured patients.
- 160 Radiation therapy undertaking patients who were scheduled to receive 2 Gy/day fraction of radiotherapy for 5 weeks or more were selected on the basis of inclusion-exclusion criteria.
- The region planned for radiotherapy treatment was breast, cervix, oral, hypo pharynx, etc.,
- The total tumor dose planned for patients was 5040 cgy.
- The approximate treatment duration was 5 weeks or more for each patient.
- Radiation has been given for 28 fractions for all the 160 patients.
- The daily tumor dose was calculated to be 180 cgy for each patient.
- All the patients were treated with EBRT (External Beam Radiotherapy)
- Out of 120 patients, 60 patients were treated with Amrad cream (Group A, to be applied twice a day) and 60 patients were treated as control Group (Group B).
- Assessment of gastro intestinal complications was done weekly by using standard RTOG scale Proforma, the grading of skin complications were done by measuring

parameters such as Erythema, Epilation, Desquamation, Pain, Pigmentation changes, Edema, and Ulceration.

- Adverse events for both the study Groups were measured during the radiotherapy treatment.
- Patient education was also provided at the initial (base) level and the patient knowledge about cancers, radiotherapy treatment, skin problems, medication use and storage before and after patient education is assessed using patient education form.

STATISTICAL ANALYSIS

The values obtained were averaged for analysis. The collected data were analyzed by ANOVA test.

8. RESULTS

Demographic data:

Population:

Out of 120 patients, 60 patients were belongs to Group A (Amrad group) and 60 patients were belongs to Group B (Untreated Control group). It is shown in (Figure 7 and Table 10).

Gender:

Among the demographic data collected for 120 patients,42 patients (35%) were male and 78 patients (65%) were female, which confirms that women are more sensitive with Radiotherapy than men (Figure 8 and Table 11).

Age:

Out of the selected 120 patients, 2 patients (2%) were in the age Group of 20- 29 years, 12 patients (10%) were in the age Group of 30 – 39 years, 28 patients (23%) were in the age Group of 40 – 49 years, 40 patients (59%) were in the age Group of 50 – 59 years, 34 patients (28%) were in the age Group of 60-69 years and 4 patients (3%) were in the age Group of 70-79 . It indicates that more number of people in the age Group of 50-59 years is affected with Radiodermatitis (Figure 9 and Table 12) among the treated population.

Social habits of the patients:

Out of the selected 120 patients, 27 patients (22%) were smokers,12 patients (10%) were tobacco users, 14 patients (12%) were alcoholics, 19 patients (16%) were betel nut chewers, 11 patients (9%) were alcoholic and smokers, 4 patients (3%) were pan chewers, 33 majority of the patients (28%) did not have any of these habits (Figure 10 and Table 13).

Type of cancer among the patients:

Out of the 120 patients, the major diagnosis are cervical cancer – 41 patients, breast cancer - 26 patients, hypo-pharynx - 5 patients, larynx - 6 patients, oral cavity, oro pharynx, rectum, ovary each contains – 4 patients, esophagus – 9 patients, cheek – 3 patients, stomach, neck, lung each contains – 3 patients, lower lip, parotid, soft palate, sub mandible, tongue, penis, fore arm and sarcoma each contains-1 patient. It indicates that cervical cancer is one of the major types of cancer that affect most of the female patients (Figure 11 and Table 14).

Tumour differentiation:

Out of 120 patients, the tumour differentiation was well in 48 patients, moderate in 64 patients and poor in 8 patients. It indicates that moderately differentiated tumour is more than the other types (Figure 12 and Table 15).

Amount of tumour dose used to the patients:

Among the 120 patients, in the radiation treatment the amount of tumour dose varies depend on the depth of the tumour, 40 gy of radiation was used to 11 patients, 50 gy was used for 72 patients, 60 gy was used for 19 patients, and 66 gy was used for 18 patients. Out of this, 50 gy of radiation was used to the maximum than the others (Figure 13 and Table 16).

Type of Therapy:

Out of 120 patients, the type of the therapy was curative to107 patients and it was palliative to 13 patients. It indicates that curative type of cancer is more likely than the palliative type (Figure 14 and Table 17).

Type of treatment:

Out of 120 patients, the treatment varies to each other depending upon their stages of cancer, surgery and radiation was given to 38 patients, chemotherapy and radiation was given to 19 patients and surgery, chemotherapy and radiation was given to 69 patients, the last treatment is preferred to the more number of patients (Figure 15 and Table 18).

Detection and diagnosis:

Out of 120 patients, the cancer is detected and diagnosed through varies detectors which mammogram was done to 22 patients, biopsy was done to 102 patients, fine needle aspiration was done by 39 patients, CT scan was done by 23 patients, USG Abdomen/pelvis was done by 52 patients, endoscopy was done by 9 patients and chest X-ray was done by 6 patients. It indicates that biopsy was used to detect the cancer efficiently (Figure 16 and Table 19).

TABLE: 10

POPULATION OF THE PATIENTS

S.No	GROUPS	NO. OF PATIENTS
1	Group A patients (Treated- Amrad Group)	60
2	Group B patients (Untreated- Control Group)	60
3	Total no. of patients	120

FIGURE: 7

POPULATION OF THE PATIENTS

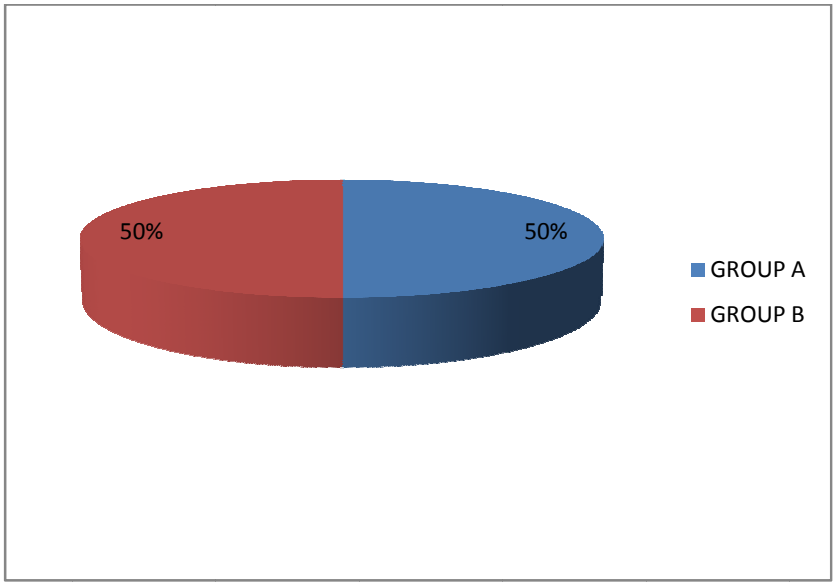


TABLE: 11

GENDERWISE DISTRIBUTION (N=120)

SEX	NUMBER OF PATIENT
MALE	42
FEMALE	78
TOTAL NUMBER OF PATIENTS	120

FIGURE: 8

GENDERWISE DISTRIBUTION (N=120)

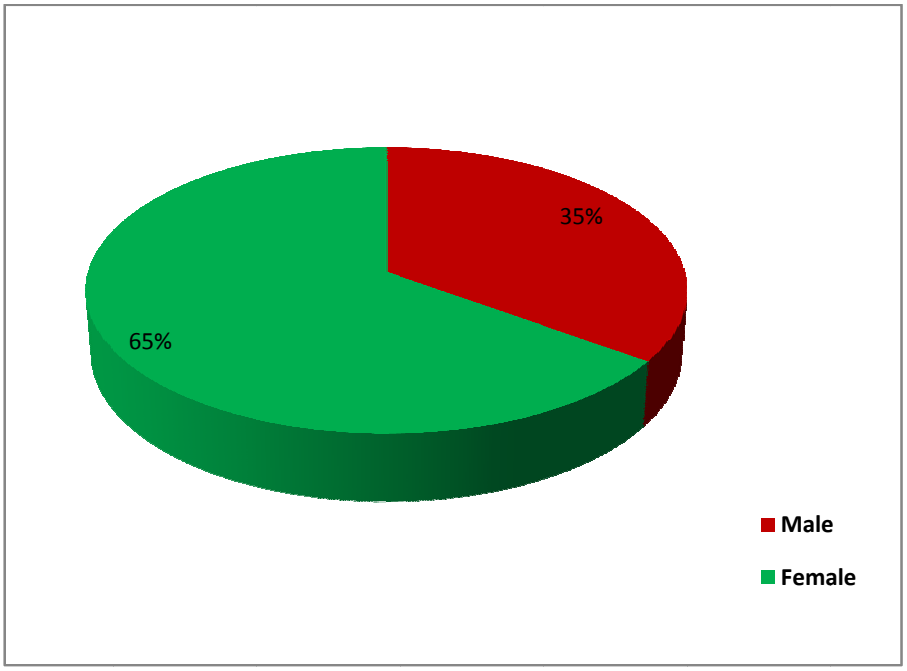


TABLE: 12

AGE WISE DISTRIBUTION (N = 120)

AGE	NUMBER OF PATIENTS
20-29	2
30-39	12
40-49	28
50-59	40
60-69	34
70-79	4

FIGURE: 9

AGE WISE DISTRIBUTION (N=120)

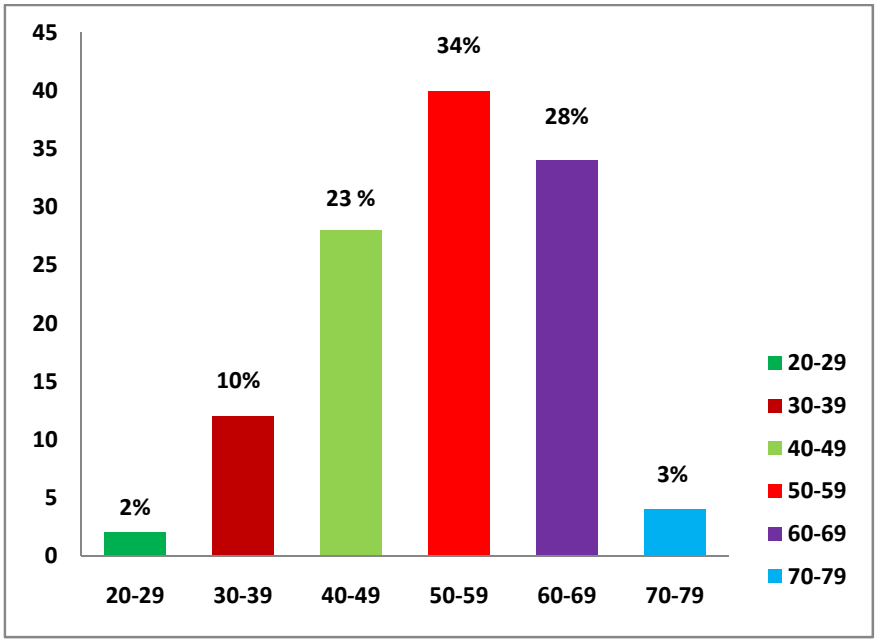


TABLE: 13

SOCIAL HABIT OF THE PATIENTS (N = 120)

SOCIAL HABITS	NUMBER OF PATIENTS
Smoking	27
Alcoholic	14
Tobacco chewing	12
Betel nut chewing	19
Smoking and alcoholic	11
Pan chewing	4
None	33

FIGURE: 10

SOCIAL HABIT OF THE PATIENTS (N = 120)

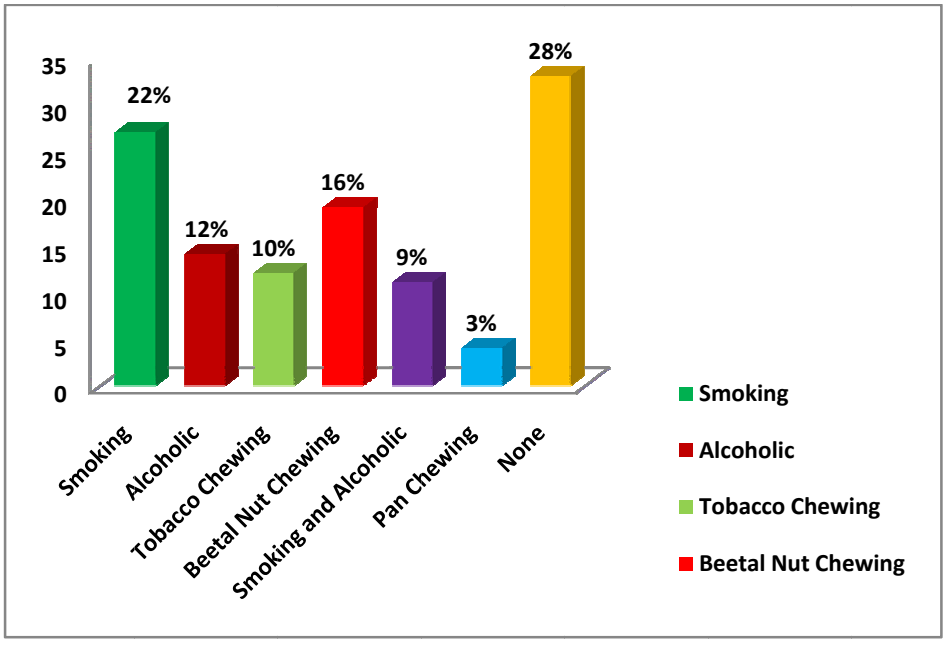


TABLE: 14

TYPE OF CANCER AMONG THE PATIENTS (N=120)

TYPE OF CANCER	NUMBER OF PATIENTS		
	Total	**Male**	**Female**
Breast	26	-	26
Cervix	41	-	41
Hypo Pharynx	5	4	1
Larynx	6	6	-
Oral cavity	4	3	1
oropharynx	4	4	-
Esophagus	9	9	-
Lower lip	1	1	-
Parotid	1	1	-
Soft palate	1	1	-
Sub mandible	1	1	-
Tongue	1	1	-
cheek	3	2	1
Rectum	4	2	2
Ovary	4	-	4
Penis	1	1	-
Stomach	2	2	-
Neck	2	2	-
Lung	2	1	1
Fore arm	1	-	1
sarcoma	1	1	-

FIGURE: 15

TYPE OF CANCER AMONG THE PATIENTS (N=120)

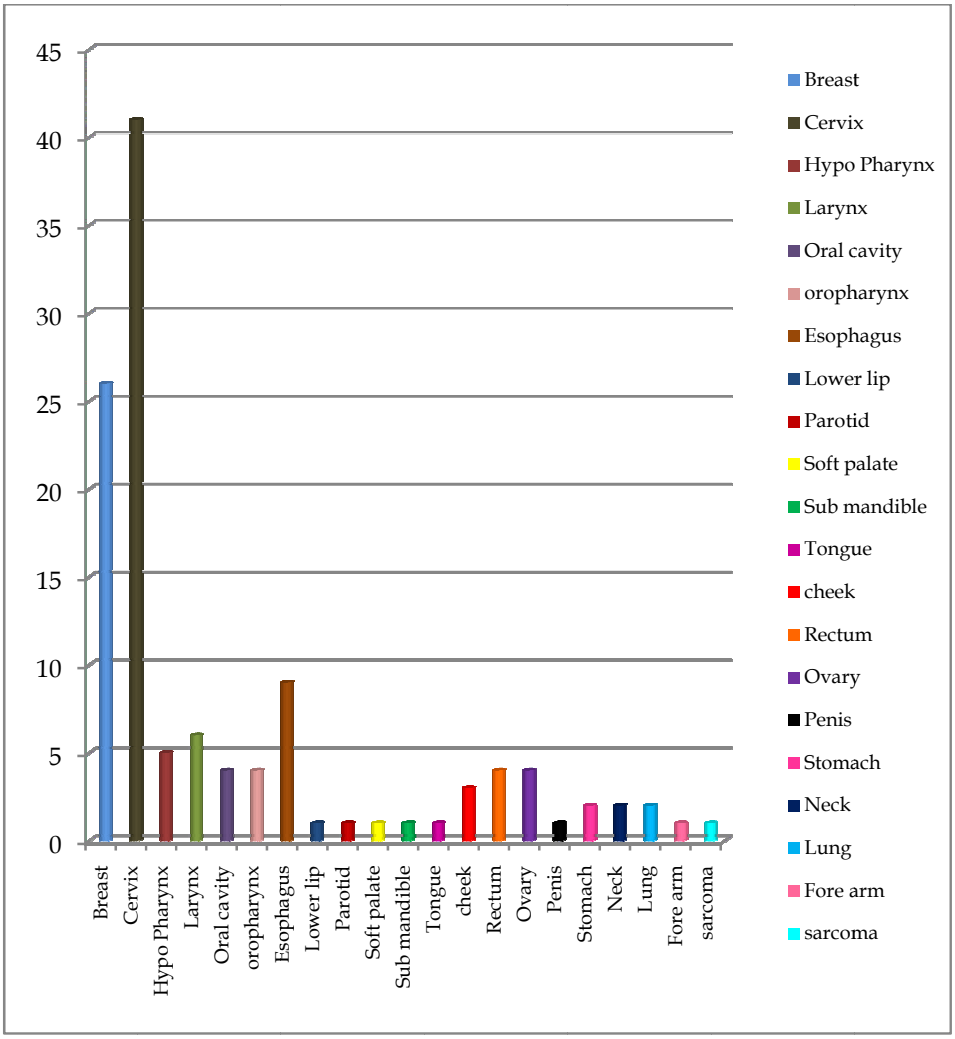


TABLE: 15

TUMOUR DIFFERENTIATION

Tumour differentiation	Number of Patients
Well defined	48
Moderate	64
Poor	8

FIGURE: 12

TUMOUR DIFFERENTIATION

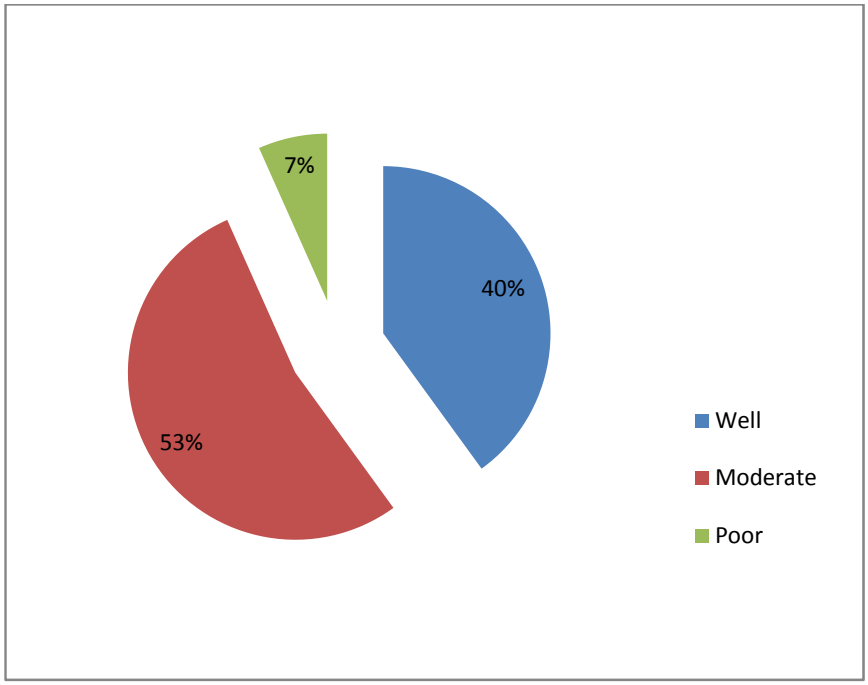


TABLE: 16

AMOUNT OF TUMOUR DOSE USED TO THE PATIENTS

Total Tumour Dose	Number of Patients
40 gy	11
50 gy	72
60 gy	19
66 gy	18

FIGURE: 13

AMOUNT OF TUMOUR DOSE USED TO THE PATIENTS

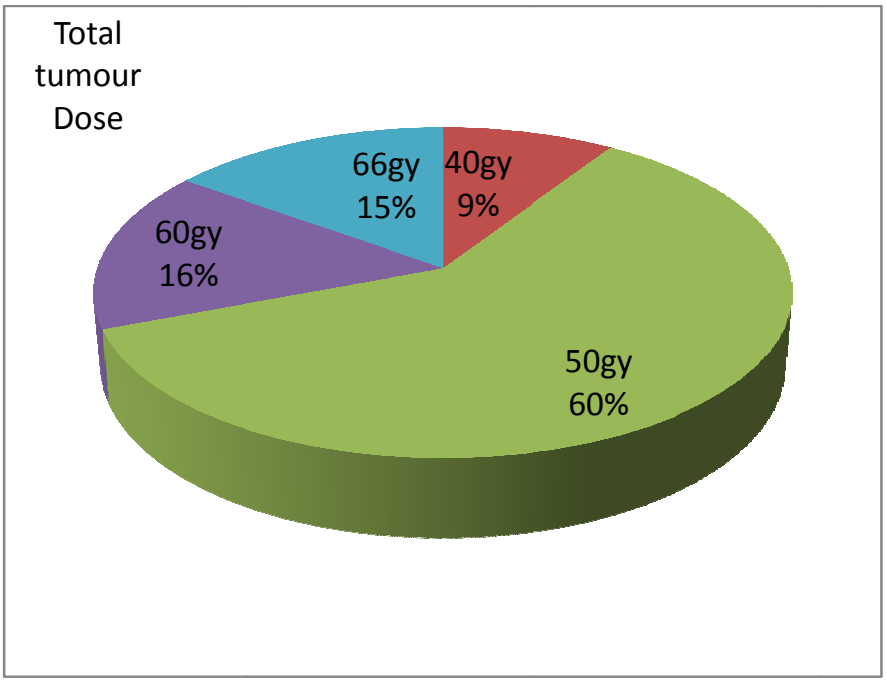


TABLE: 17

TYPE OF THERAPY

THERAPY	NUMBER OF PATIENTS
Curative	107
Palliative	13

FIGURE: 14

TYPE OF THERAPY

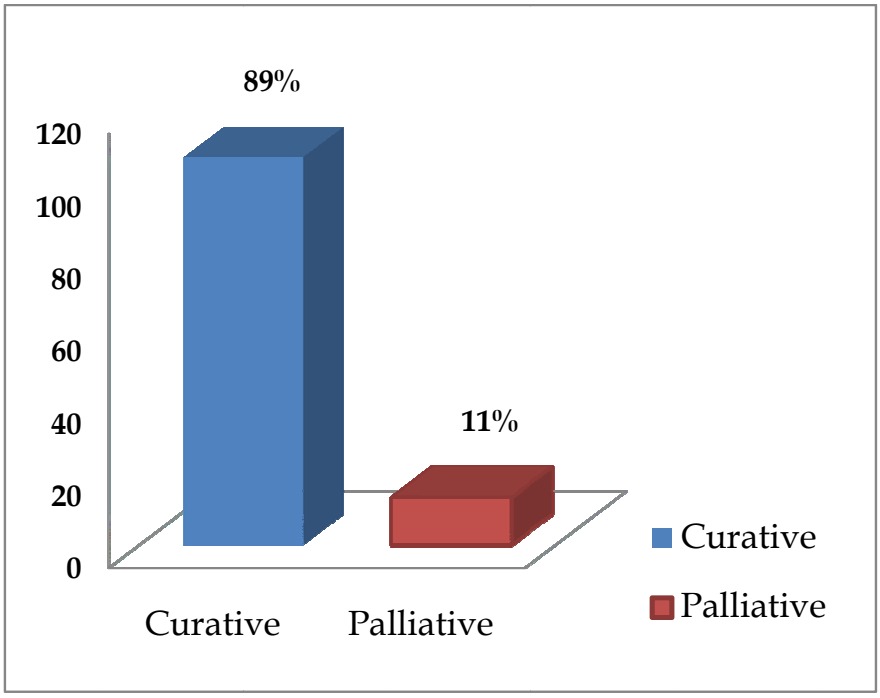


TABLE: 18

TYPE OF TREATMENT

Type of Treatment	Number of patients
Surgery+Radiotherapy	38
Chemotherapy+Radiation	19
Surgery+chemo+Radiation	69

FIGURE: 15

TYPE OF TREATMENT

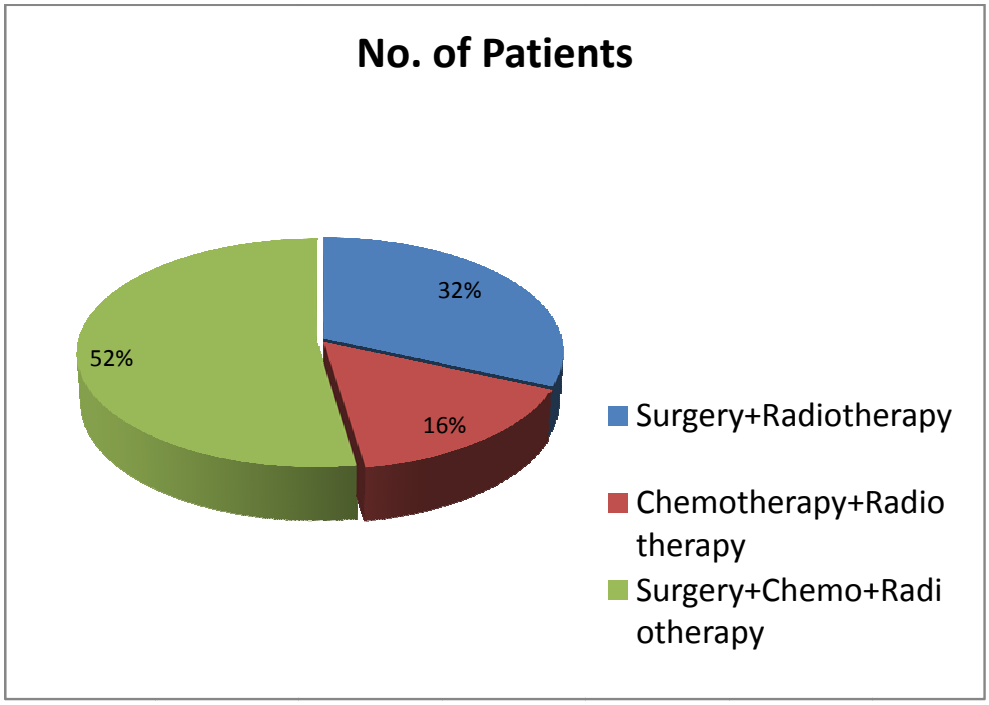


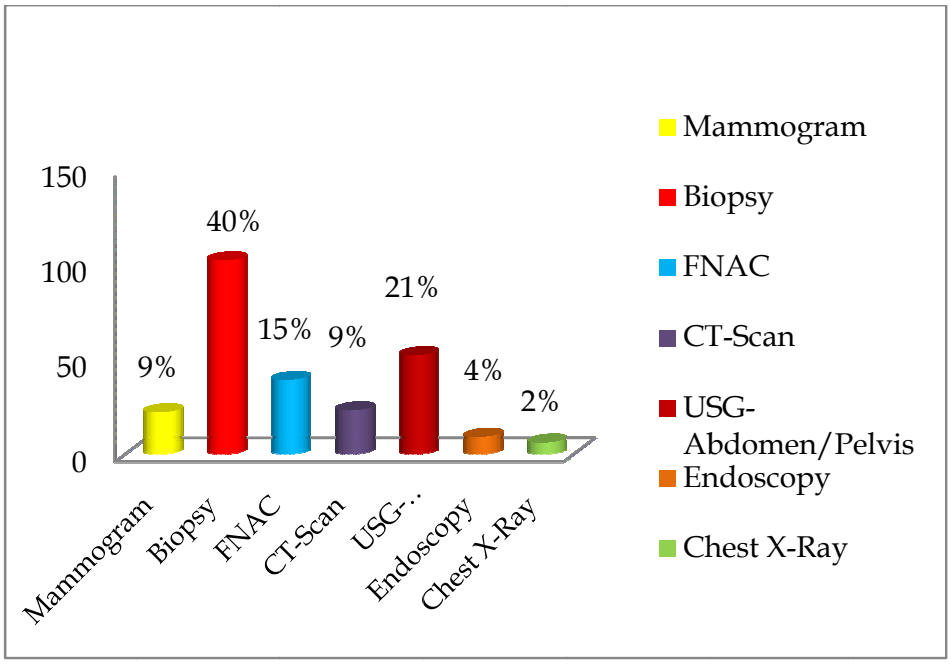
TABLE: 19

DETECTION AND DIAGNOSIS

Detection And Diagnosis	Number of patients
Mammogram	22
Biopsy	102
FNAC	39
CT-Scan	23
USG-Abdomen/pelvis	52
Endoscopy	9
Chest X-Ray	6

FIGURE: 16

DETECTION AND DIAGNOSIS



Comparative data:

Erythema:

From Figure 17 and Table 20, it is well indicated that the erythema score among Group A patients (63.08) was less than that of Group B (129.09). It clearly shows that the possibility for erythema among Group A patients has been decreased than that for Group B patients. The mean score is found to be much less in Group A 0.13 ± 0.20 as compared to Group B 0.84 ± 0.55. Both groups show statistically significant difference by student t test.

FIGURE 17: ERYTHEMA

MEAN SCORE FOR ERYTHEMA IN GROUP A AND GROUP B PATIENTS

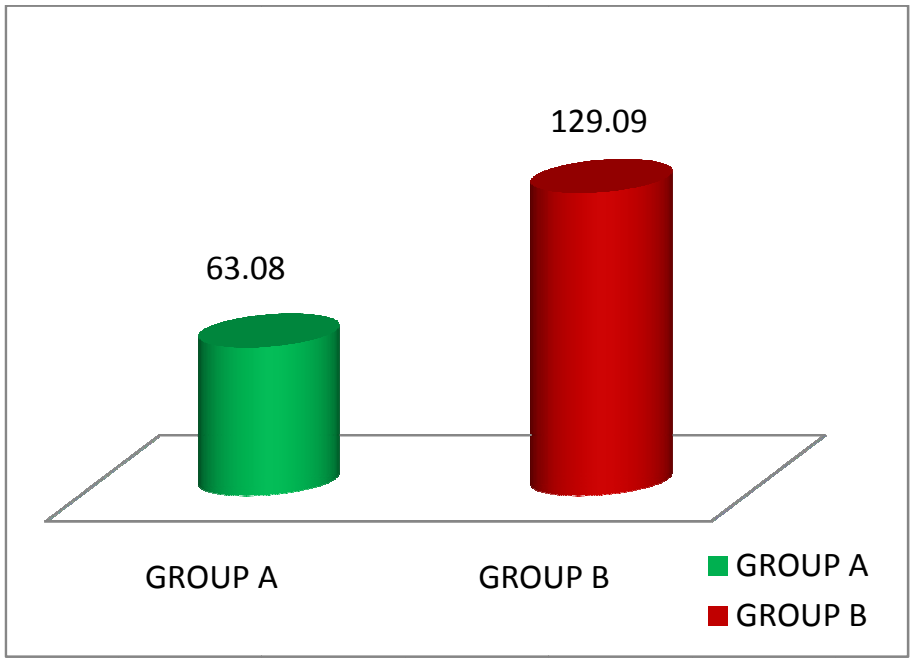


TABLE: 20

MEAN SCORE FOR ERYTHEMA IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for Group A	Patient ID	Mean score for Group B
A1	0.82	B1	2.25
A2	1.35	B2	2.17
A3	1.14	B3	2.25
A4	1.14	B4	2.92
A5	0.82	B5	2.21
A6	1.03	B6	2.28
A7	1	B7	2.1
A8	1.07	B8	2.07
A9	1.25	B9	2.5
A10	1.21	B10	2
A11	1	B11	2.28
A12	1.28	B12	3.5
A13	1.17	B13	3
A14	1	B14	3.89
A15	1.62	B15	2.35
A16	0.35	B16	2.17
A17	1.74	B17	2.75
A18	1.4	B18	2.92
A19	0.92	B19	2.31
A20	1.53	B20	2.28
A21	1	B21	2.01
A22	1.7	B22	2.07
A23	1.75	B23	2.5
A24	1.21	B24	1
A25	1	B25	2.68
A26	1.48	B26	3.5
A27	1.97	B27	3
A28	1	B28	3.39
A29	0.24	B29	2.5
A30	1.36	B30	2.7

A31	1.18	B31	2.50
A32	1.14	B32	2.27
A33	0.78	B33	2.41
A34	1.34	B34	2.08
A35	1	B35	2.1
A36	1.87	B36	2.37
A37	1.85	B37	2.1
A38	1.01	B38	2
A39	1	B39	2.58
A40	1.58	B40	3.7
A41	1.07	B41	3
A42	1	B42	3.59
A43	0.52	B43	2.65
A44	1.45	B44	2.37
A45	1.44	B45	2.75
A46	1.74	B46	2.82
A47	0.32	B47	2.61
A48	1.83	B48	2.68
A49	1	B49	2.1
A50	1.97	B50	2.87
A51	1.05	B51	2.9
A52	1.21	B52	2
A53	1	B53	2.28
A54	1.48	B54	3.6
A55	1.77	B55	3
A56	1.42	B56	2.42
A57	1	B57	2.18
A58	1.52	B58	3.2
A59	1	B59	3.23
A60	0.83	B60	3.99
TOTAL	**63.08**	**TOTAL**	**129.09**
MEAN ± SD	**0.1317 ± 0.2053**	**MEAN ± SD**	**0.8371± 0.5597**
P Value highly significant* <0.0001**			

Epilation:

The epilation score for the Group A patients (25.24) was less than that of Group B (34.31). The mean score is found to be much less in Group A 0.42 ± 0.19 as compared to Group B 0.57 ± 0.28. Both groups show statistically significant difference by student t test. It is shown in Figure 18 and Table 21.

FIGURE 18: EPILATION

MEAN SCORE FOR EPILATION IN GROUP A AND GROUP B PATIENTS

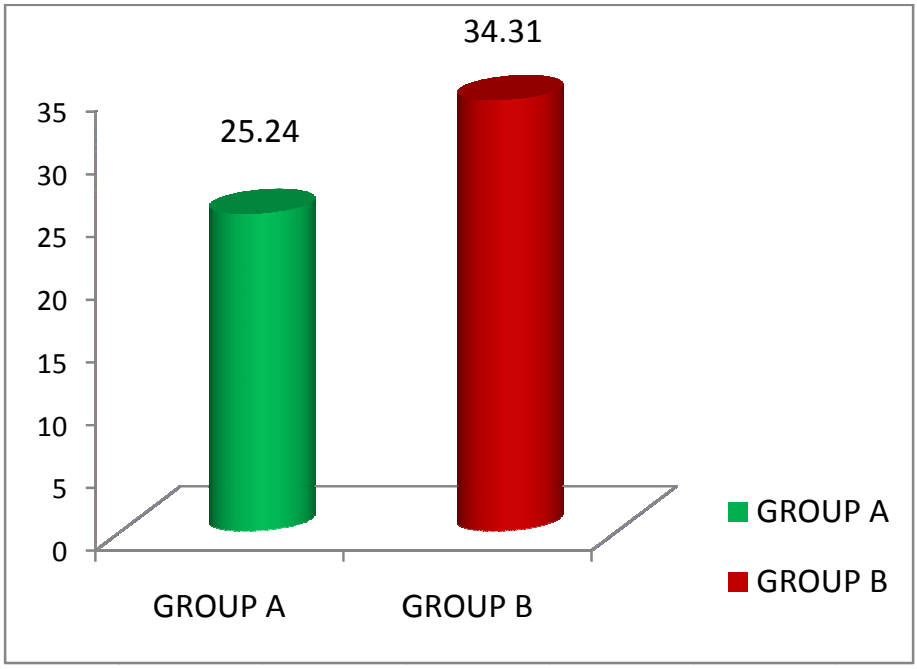


TABLE: 21

MEAN SCORE FOR EPILATION IN GROUP A AND

GROUP B PATIENTS

Patient ID	Mean score for Group A	Patient ID	Mean score for Group B
A1	0.27	B1	0.46
A2	0.29	B2	0.35
A3	0.25	B3	0.43
A4	0.45	B4	0.45
A5	0.56	B5	0.65
A6	0.5	B6	0.36
A7	0.25	B7	0.23
A8	0.5	B8	0.24
A9	0.5	B9	0.22
A10	0.25	B10	0.26
A11	0.42	B11	0.15
A12	0.45	B12	0.28
A13	0.45	B13	0.25
A14	0.65	B14	0.26
A15	0.35	B15	0.25
A16	0.37	B16	0.42
A17	0.16	B17	0.5
A18	0.23	B18	0.82
A19	0.24	B19	0.84
A20	0.22	B20	1
A21	0.12	B21	0.5
A22	1	B22	0.5
A23	0.23	B23	0.5
A24	0.44	B24	0.55
A25	0.43	B25	0.65
A26	0.27	B26	0.66
A27	0.34	B27	0.68
A28	0.45	B28	0.25
A29	0.43	B29	0.54
A30	0.42	B30	0.48

A31	0.5	B31	0.44
A32	0.82	B32	1
A33	0.84	B33	1
A34	1	B34	1
A35	0.5	B35	1
A36	0.5	B36	1
A37	0.5	B37	1
A38	0.55	B38	1
A39	0.65	B39	1
A40	0.66	B40	1
A41	0.68	B41	1
A42	0.25	B42	1
A43	0.54	B43	1
A44	0.48	B44	1
A45	0.44	B45	1
A46	0.46	B46	0.27
A47	0.35	B47	0.29
A48	0.43	B48	0.25
A49	0.45	B49	0.45
A50	0.65	B50	0.56
A51	0.36	B51	0.5
A52	0.23	B52	0.25
A53	0.24	B53	0.5
A54	0.22	B54	0.5
A55	0.26	B55	0.25
A56	0.15	B56	0.42
A57	0.28	B57	0.45
A58	0.25	B58	0.45
A59	0.26	B59	0.65
A60	0.25	B60	0.35
TOTAL	**25.24**	**TOTAL**	**34.31**
MEAN ± SD	**0.4206±0.1936**	**MEAN ± SD**	**0.5718±0.2871**
P Value highly significant* <0.0001**			

Edema:

The comparative study shows that the total score for edema among Group A patients (0.99) was less than that of Group B (13.3). The mean score is found to be much less in Group A 0.08 ± 0.03 as compared to Group B 0.09 ± 0.28. Both groups show statistically significant difference by student t test. It is shown in Figure 19 and Table 22.

FIGURE 19: OEDEMA

MEAN SCORE FOR OEDEMA IN GROUP A AND GROUP B PATIENTS

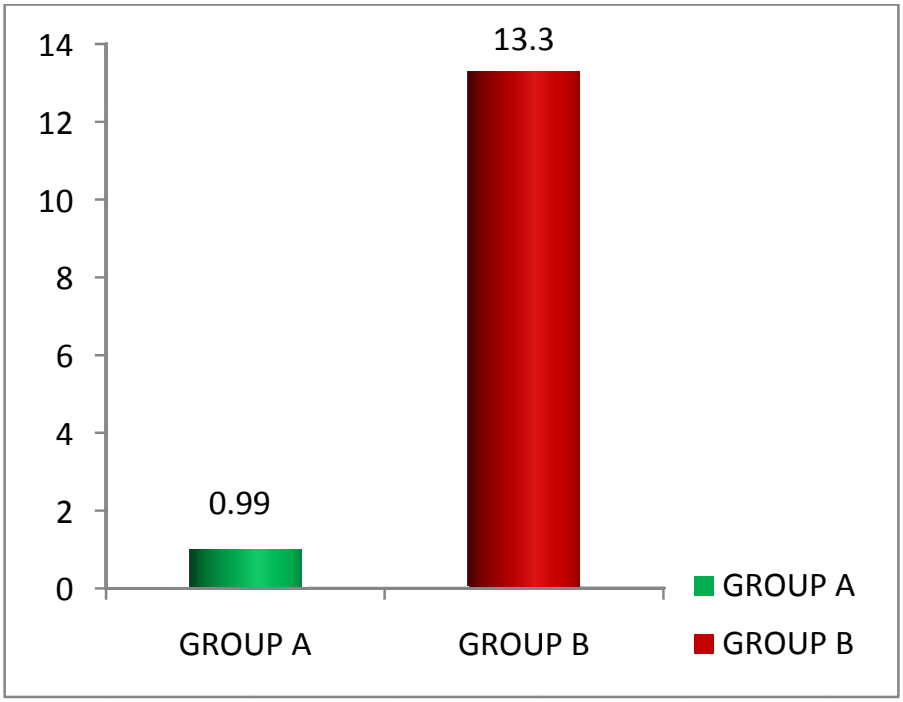


TABLE: 22

MEAN SCORE FOR OEDEMA IN GROUP A AND

GROUP B PATIENTS

Patient ID	Mean score for group A	Patient ID	Mean score for group B
A1	0	B1	0
A2	0	B2	1
A3	0	B3	0
A4	0	B4	0
A5	0	B5	0
A6	0	B6	1.6
A7	0	B7	0
A8	0	B8	0
A9	0.11	B9	0
A10	0	B10	0
A11	0	B11	0
A12	0	B12	0
A13	0.17	B13	1.5
A14	0	B14	0
A15	0	B15	0
A16	0	B16	0
A17	0	B17	1
A18	0	B18	0
A19	0	B19	0
A20	0	B20	0
A21	0	B21	1.65
A22	0.14	B22	0
A23	0	B23	0
A24	0	B24	0
A25	0	B25	1
A26	0	B26	0
A27	0	B27	0
A28	0	B28	0
A29	0	B29	0
A30	0	B30	1.8

A31	0	B31	0
A32	0	B32	0
A33	0.3	B33	0
A34	0	B34	0
A35	0	B35	0
A36	0	B36	0
A37	0	B37	0
A38	0	B38	1
A39	0	B39	0
A40	0	B40	0
A41	0	B41	0
A42	0.11	B42	0
A43	0	B43	0
A44	0	B44	0
A45	0	B45	0
A46	0	B46	1
A47	0	B47	0
A48	0	B48	0
A49	0	B49	0
A50	0.16	B50	0
A51	0	B51	0
A52	0	B52	0
A53	0	B53	0
A54	0	B54	0
A55	0	B55	0
A56	0	B56	0
A57	0	B57	1.75
A58	0	B58	0
A59	0	B59	0
A60	0	B60	0
TOTAL	**0.99**	**TOTAL**	**13.3**
MEAN±SD	**0.0804±0.0333**	**MEAN±SD**	**0.0983±0.2808**
P Value highly significant* <0.0001**			

Pain:

From the selected 120 patients,the total score for pain for Group A patients (19.19) was found to be less than that of Group B (33.83). The mean score is found to be much less in Group A 0.31 ± 0.43 as compared to Group B 0.56 ± 0.69. Both groups show statistically significant difference by student t test. It is shown in Figure 20 and Table 23.

FIGURE 20: PAIN

MEAN SCORE FOR PAIN IN GROUP A AND GROUP B PATIENTS

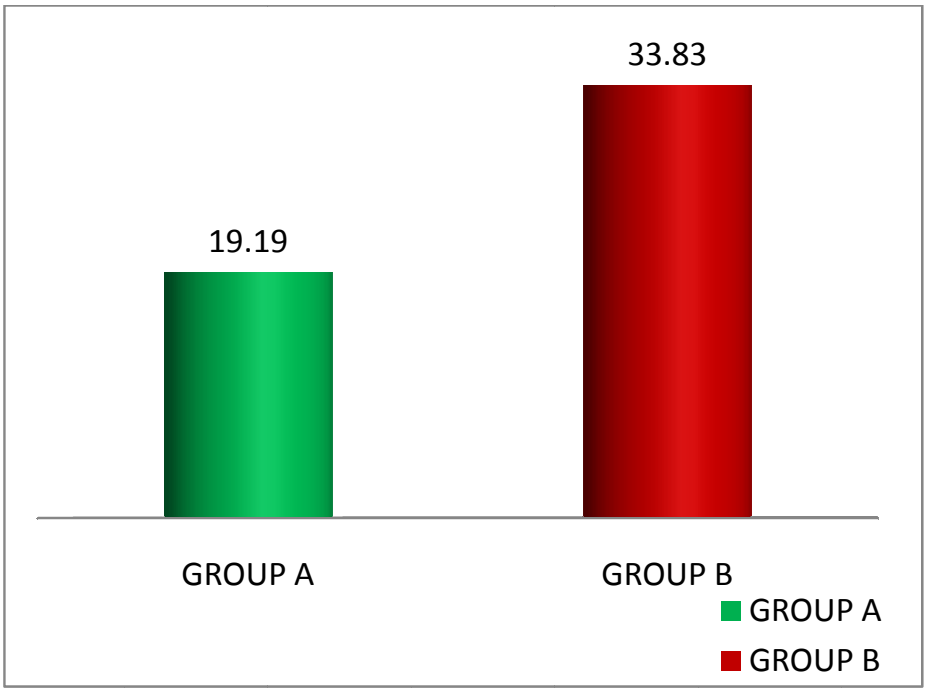


TABLE: 23

MEAN SCORE FOR PAIN IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for group A	Patient ID	Mean score for group B
A1	0.25	B1	1
A2	0.25	B2	1
A3	0.19	B3	1
A4	0.2	B4	0
A5	0	B5	1.5
A6	0	B6	1.39
A7	0	B7	1.25
A8	0	B8	0
A9	0.34	B9	0
A10	0.45	B10	1
A11	0.42	B11	0
A12	0	B12	0
A13	0.5	B13	0
A14	0.33	B14	0
A15	0.15	B15	1.2
A16	0	B16	1.5
A17	0	B17	0
A18	0.12	B18	0
A19	0.5	B19	0
A20	0.42	B20	0
A21	0.24	B21	1
A22	0.55	B22	0
A23	0	B23	0
A24	0	B24	0
A25	0	B25	1.6
A26	0	B26	0
A27	1	B27	0
A28	0	B28	0
A29	0	B29	1
A30	0	B30	0

A31	0	B31	0
A32	0.2	B32	0
A33	1.5	B33	0
A34	1.34	B34	1.9
A35	1.5	B35	1.67
A36	1	B36	0
A37	1	B37	1.45
A38	0	B38	1.55
A39	0	B39	1
A40	0	B40	0
A41	0	B41	0
A42	0	B42	0
A43	0.15	B43	1
A44	0.13	B44	0
A45	0.24	B45	0
A46	1	B46	0
A47	0.31	B47	2
A48	0.34	B48	2.1
A49	0.2	B49	1.72
A50	0	B50	0
A51	0	B51	0
A52	0	B52	1
A53	1	B53	0
A54	0	B54	0
A55	0	B55	0
A56	0.62	B56	0
A57	1	B57	1
A58	1.5	B58	1
A59	0	B59	1
A60	0.25	B60	1
TOTAL	**19.19**	**TOTAL**	**33.83**
MEAN±SD	**0.3198±0.4341**	**MEAN±SD**	**0.5638±0.6912**
P Value highly significant* <0.0001**			

Desquamation:

The total score for desquamatiom for Group A patients (7.37) was less than that of Group B (22.09). The mean score is found to be much less in Group A 0.12 ± 0.29 as compared to Group B 0.36 ± 0.50. Both groups show statistically significant difference by student t test. It is shown in Figure 21 and Table 24.

FIGURE 21: DESQUAMATION

MEAN SCORE FOR DESQUAMATION IN GROUP A AND GROUP B PATIENTS

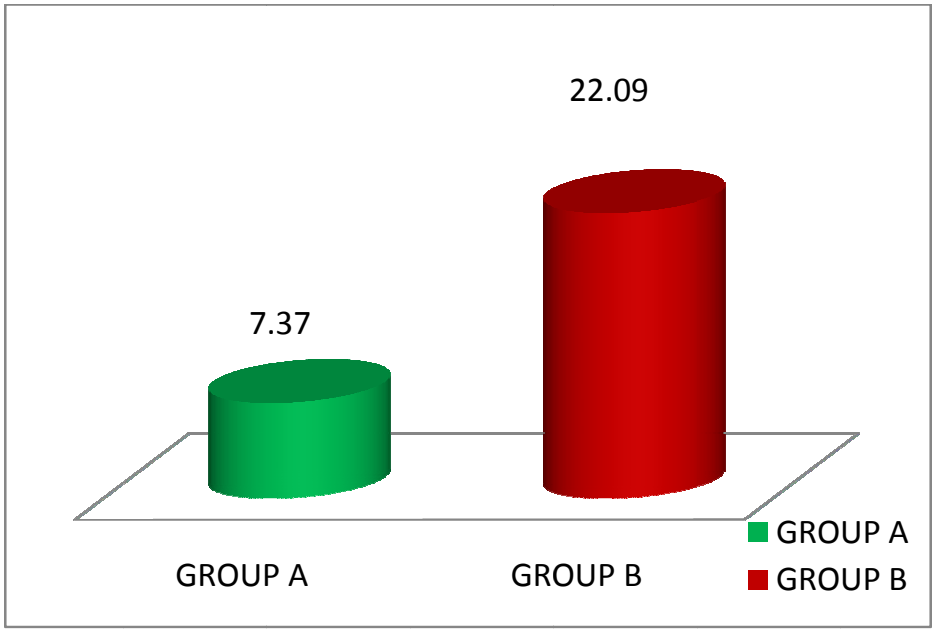


TABLE: 24

MEAN SCORE FOR DESQUAMATION IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for group A	Patient ID	Mean score for group B
A1	0.23	B1	1
A2	0.21	B2	1
A3	0	B3	0.5
A4	0	B4	1
A5	1.5	B5	0
A6	1.2	B6	0
A7	0	B7	1.65
A8	0	B8	0
A9	0	B9	0
A10	0.15	B10	0
A11	0.2	B11	1.25
A12	0.5	B12	0
A13	0.25	B13	0
A14	0	B14	0
A15	0	B15	1
A16	0	B16	0.23
A17	0	B17	0
A18	0	B18	0
A19	0	B19	0
A20	0	B20	0
A21	0	B21	0
A22	0	B22	0
A23	0	B23	1.5
A24	0	B24	0
A25	0	B25	0
A26	0	B26	0
A27	0	B27	0
A28	0	B28	0
A29	0	B29	1
A30	0	B30	1

A31	1	B31	1
A32	0	B32	0
A33	0	B33	0
A34	0	B34	0
A35	0	B35	0
A36	0	B36	0
A37	0	B37	0
A38	0	B38	0.65
A39	0	B39	0
A40	0	B40	1
A41	0	B41	1
A42	0.45	B42	1
A43	0.3	B43	0
A44	0.46	B44	0
A45	0	B45	0
A46	0	B46	0.82
A47	0	B47	0.54
A48	0.62	B48	1
A49	0	B49	1
A50	0	B50	1
A51	0	B51	0
A52	0	B52	0
A53	0.3	B53	0
A54	0	B54	0
A55	0	B55	0.95
A56	0	B56	0
A57	0	B57	0
A58	0	B58	0
A59	0	B59	0
A60	0	B60	1
TOTAL	**7.37**	**TOTAL**	**22.09**
MEAN±SD	**0.1228±0.2978**	**MEAN±SD**	**0.3681±0.5041**
P Value highly significant* <0.0001**			

Pigmentaion changes:

The total score for pigmantation changes Group A patients (32.29) was less than that of Group B (39.54). The mean score is found to be much less in Group A 0.53 ± 0.42 as compared to Group B 0.65 ± 0.41. Both groups show statistically significant difference by student t test. It is shown in Figure 22 and Table 25.

FIGURE 22: PIGMENTATION CHANGES

MEAN SCORE FOR PIGMENTATION CHANGES IN GROUP A AND GROUP B PATIENTS

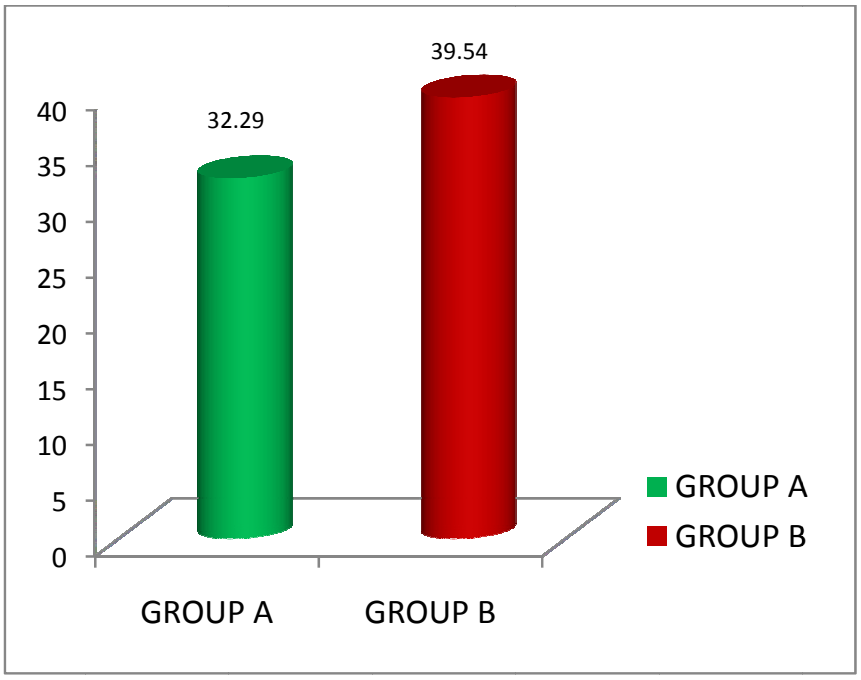


TABLE: 25

MEAN SCORE FOR PIGMENTATION CHANGES IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for Group A	Patient ID	Mean score for Group B
A1	0.5	B1	0.12
A2	0.12	B2	0.2
A3	0.25	B3	0.1
A4	0.5	B4	1
A5	1	B5	1
A6	1	B6	1
A7	0	B7	1
A8	1	B8	0.5
A9	0.65	B9	1
A10	0.45	B10	0
A11	0	B11	1
A12	0	B12	1
A13	0	B13	0.2
A14	0	B14	0.15
A15	1	B15	0.12
A16	1	B16	0.1
A17	1	B17	0.3
A18	1	B18	0.23
A19	1	B19	0
A20	0.2	B20	1
A21	0.23	B21	1
A22	0.26	B22	1
A23	0.24	B23	1
A24	0.14	B24	1
A25	0.5	B25	1
A26	0.8	B26	0.2
A27	0.54	B27	0.1
A28	0	B28	0.32
A29	0	B29	0.22
A30	0	B30	0.1

A31	0	B31	0.2
A32	1	B32	0.5
A33	0	B33	1
A34	0	B34	1
A35	0	B35	0.55
A36	0	B36	0.6
A37	0	B37	1
A38	0	B38	1
A39	0	B39	0.3
A40	0	B40	1
A41	0	B41	0
A42	0	B42	0
A43	0	B43	1.45
A44	1	B44	1
A45	0	B45	1
A46	0	B46	0
A47	0	B47	1
A48	0	B48	0.54
A49	0	B49	0.65
A50	0	B50	0.23
A51	0	B51	0.43
A52	0	B52	0.56
A53	0.23	B53	1.9
A54	0	B54	0
A55	0	B55	1
A56	0	B56	2
A57	0.25	B57	1
A58	0	B58	1
A59	0	B59	1
A60	0	B60	1
TOTAL	**32.295**	**TOTAL**	**39.54**
MEAN ± SD	**0.5382±0.4295**	**MEAN ± SD**	**0.659±0.4125**
P Value highly significant* <0.0001**			

Telangiecasia:

The total score for telangiecasia from the beginning of the treatment for Group A patients (4.39) was less than that of Group B (40.42). The mean score is found to be much less in Group A 0.07 ± 0.22 as compared to Group B 0.67 ± 0.52. Both groups show statistically significant difference by student t test. It is shown in Figure 23 and Table 26.

FIGURE: 23 TELANGIECTASIA
MEAN SCORE FOR TELANGIECTASIA IN GROUP A AND GROUP B PATIENTS

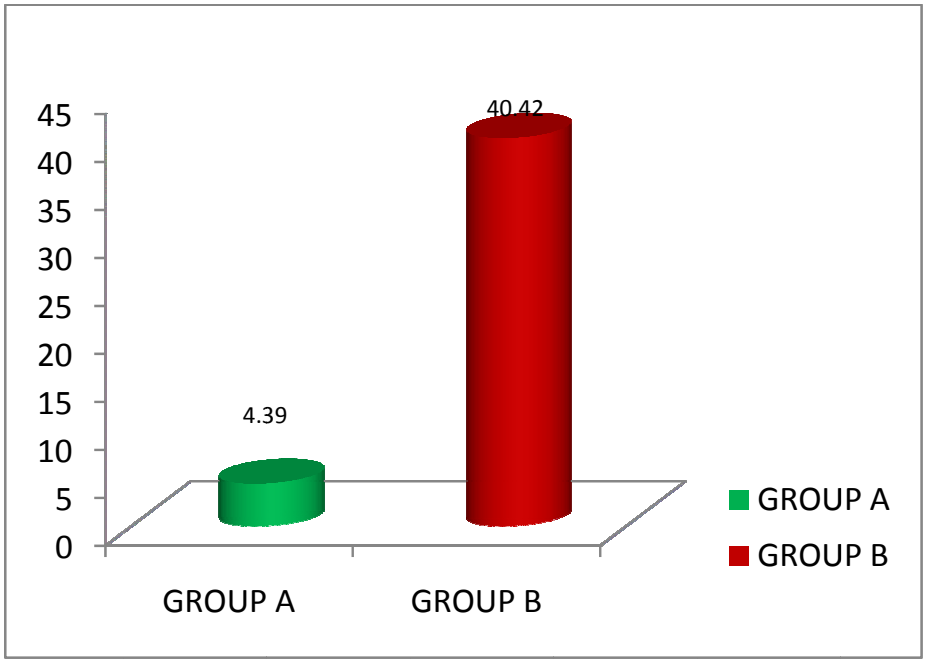


TABLE: 26

MEAN SCORE FOR TELANGIECTASIA IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for Group A	Patient ID	Mean score for Group B
A1	0	B1	1
A2	0	B2	1
A3	0	B3	1
A4	0.3	B4	1
A5	0	B5	1
A6	0	B6	0.24
A7	0	B7	0.2
A8	0	B8	0.5
A9	0.23	B9	0.66
A10	0	B10	0.54
A11	0	B11	1
A12	0	B12	1.23
A13	0	B13	1
A14	0	B14	0
A15	1	B15	0
A16	0	B16	0
A17	0	B17	1.65
A18	0	B18	1
A19	0	B19	0
A20	0	B20	0
A21	0	B21	0.54
A22	0.12	B22	0.34
A23	0.14	B23	1
A24	0.124	B24	0
A25	0	B25	0
A26	0	B26	1.9
A27	0	B27	0.2
A28	0	B28	0.24
A29	0	B29	0
A30	0	B30	0.27

A31	0	B31	0.2
A32	1	B32	0.5
A33	0	B33	1
A34	0	B34	1
A35	0	B35	0.55
A36	0	B36	0.6
A37	0	B37	1
A38	0	B38	1
A39	0	B39	0.3
A40	0	B40	1
A41	0	B41	0
A42	0	B42	0
A43	0	B43	1.45
A44	1	B44	1
A45	0	B45	1
A46	0	B46	0
A47	0	B47	1
A48	0	B48	0.54
A49	0	B49	0.65
A50	0	B50	0.23
A51	0	B51	0.43
A52	0	B52	0.56
A53	0.23	B53	1.9
A54	0	B54	0
A55	0	B55	1
A56	0	B56	2
A57	0.25	B57	1
A58	0	B58	1
A59	0	B59	1
A60	0	B60	1
TOTAL	**4.394**	**TOTAL**	**40.42**
MEAN ± SD	**0.0732±0.2249**	**MEAN ± SD**	**0.6736±0.5254**
P Value highly significant* <0.0001**			

Ulceration:

The total score for ulceration in Group A patients (1.45) were less than that of Group B (34.7). The mean score is found to be much less in Group A 0.02 ± 0.78 as compared to Group B 0.57 ± 0.54. Both groups show statistically significant difference by student t test. It is shown in Figure 24 and Table 27.

FIGURE: 24 ULCERATION

MEAN SCORE FOR ULCERATION IN GROUP A AND GROUP B PATIENTS

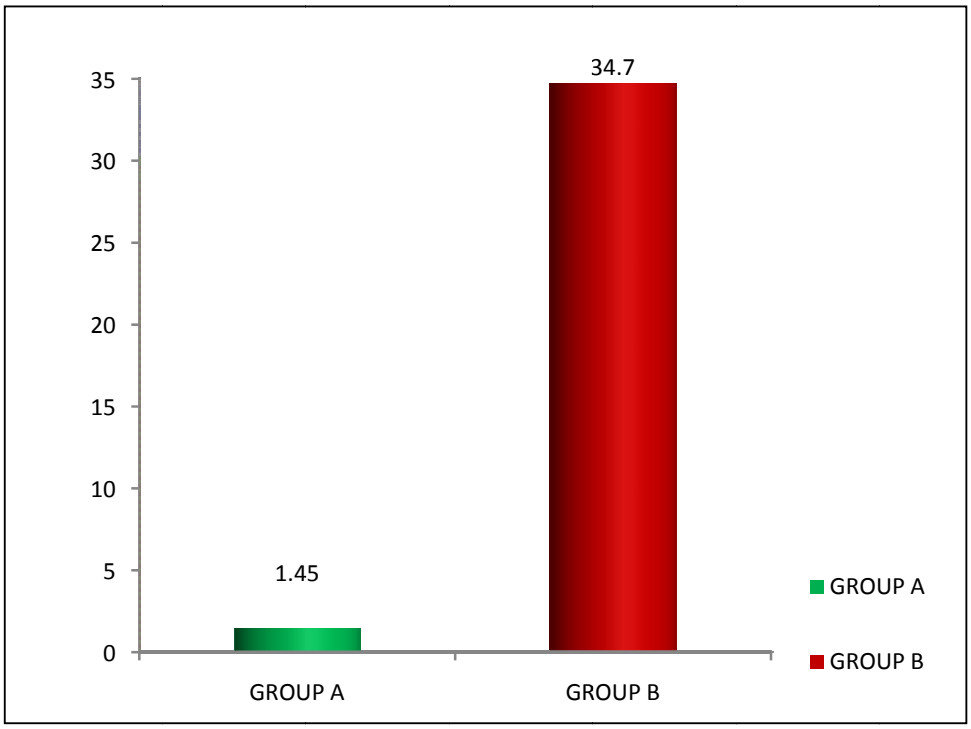


TABLE: 27

MEAN SCORE FOR ULCERATION IN GROUP A AND GROUP B PATIENTS

Patient ID	Mean score for group A	Patient ID	Mean score for group B
A1	0	B1	1
A2	0	B2	1
A3	0	B3	1
A4	0	B4	1
A5	0	B5	0
A6	0	B6	0
A7	0.1	B7	0
A8	0.09	B8	0
A9	0	B9	0
A10	0	B10	0
A11	0	B11	0.25
A12	0	B12	0
A13	0	B13	0
A14	0	B14	0
A15	0.1	B15	0
A16	0.085	B16	1
A17	0	B17	0
A18	0	B18	0
A19	0	B19	0
A20	0	B20	1
A21	0	B21	1
A22	0	B22	1
A23	0.09	B23	1
A24	0	B24	1
A25	0	B25	0
A26	0	B26	0
A27	0	B27	0
A28	0	B28	0
A29	0	B29	1.5
A30	0	B30	1

A31	0	B31	1
A32	0.16	B32	1.05
A33	0	B33	1
A34	0	B34	1
A35	0	B35	1
A36	0	B36	1
A37	0	B37	1
A38	0	B38	1
A39	0	B39	0.6
A40	0	B40	1
A41	0	B41	1
A42	0	B42	0
A43	0.15	B43	0
A44	0	B44	0
A45	0	B45	0
A46	0	B46	0
A47	0	B47	0
A48	0	B48	1
A49	0	B49	1
A50	0	B50	1
A51	0	B51	1
A52	0	B52	2.1
A53	0	B53	0
A54	0.54	B54	0
A55	0	B55	0
A56	0	B56	1.2
A57	0	B57	1
A58	0	B58	1
A59	0	B59	1
A60	0.14	B60	1
TOTAL	**1.455**	**TOTAL**	**34.7**
MEAN±SD	**0.0242±.0789**	**MEAN±SD**	**0.5783±0.5455**

Cumulative score analysis:

Table 28, Figure 25 & 26 shows the overall toxicity scores of all the parameters among Group A (Amrad cream) and Group B (Untreated Control).The mean and standard deviation of both the group were found to be **6.85 ± 2.6877** and **14.76 ± 4.1451** respectively. Both groups show statistically significant difference by student t test.

The mean of toxicity evaluation grading for Group A (Amrad) and Group B (Control) were found to be 0.88 and 2.25 respectively. This shows that the drug is more effective than control.

Figure: 25

OVERALL MEAN SCORE FOR SKIN REACTIONS

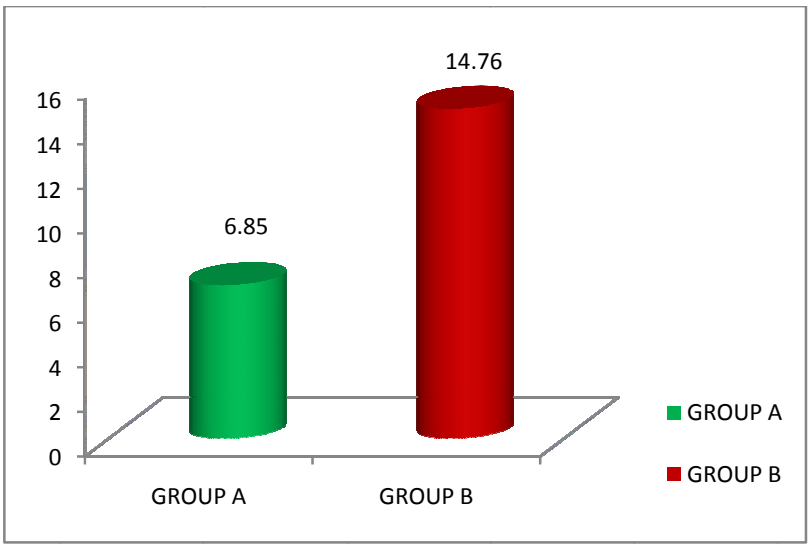


Figure: 26

MEAN TOXICITY GRADE FOR SKIN REACTIONS

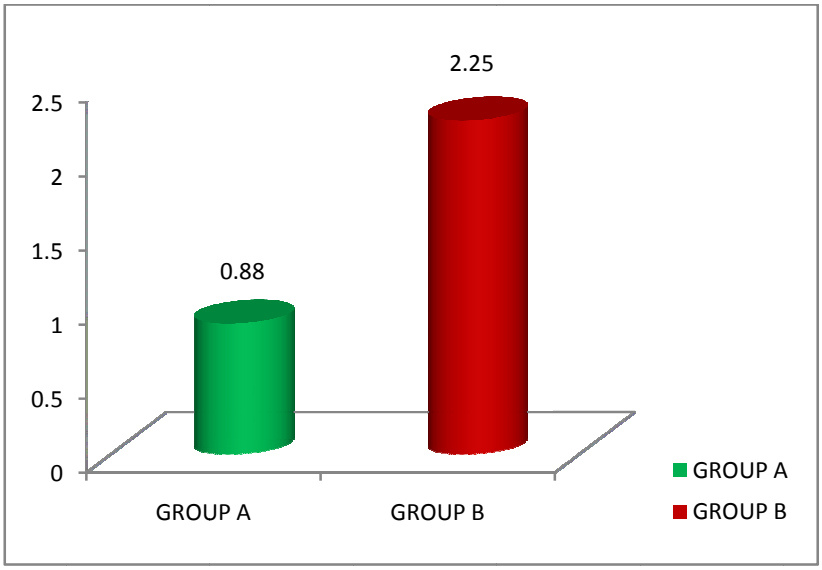


TABLE: 28

OVERALL MEAN TOXICITY SCORE FOR SKIN REACTIONS

Patient ID	Total score of all the parameters (group A)	Toxicity evaluation grading	Patient ID	Total score of all the parameters (group B)	Toxicity evaluation grading
A1	2.8	1	B1	11.4	2
A2	2.5	1	B2	10.6	2
A3	9.72	1	B3	13.6	2
A4	8.28	1	B4	17.78	2
A5	9.37	1	B5	12.76	2
A6	7.36	1	B6	13.5	2
A7	7.87	1	B7	10.9	2
A8	7.43	1	B8	9.8	2
A9	5.34	1	B9	8.75	1
A10	1.96	0	B10	15.4	2
A11	3.56	1	B11	14.7	2
A12	4.43	1	B12	15.8	2
A13	4.87	1	B13	18.6	3
A14	6.34	1	B14	16.76	2
A15	5.43	1	B15	15.89	2
A16	6.23	1	B16	9.16	2
A17	7.54	1	B17	14.56	2
A18	9.5	1	B18	18	2
A19	1.65	0	B19	11.5	2
A20	4.15	1	B20	10.66	2
A21	7.28	1	B21	11.54	2
A22	9.7	1	B22	13	2
A23	6.91	1	B23	16.7	2
A24	9.5	1	B24	8.8	1
A25	5.55	1	B25	14.3	2
A26	7.5	1	B26	12.2	2
A27	0.96	0	B27	14.5	2
A28	4.98	1	B28	15.24	2
A29	5.2	1	B29	16.65	2
A30	9.26	1	B30	11.55	2

A31	9.35	1	B31	18.5	3
A32	7.68	1	B32	19.55	3
A33	6.87	1	B33	18.77	3
A34	1.55	0	B34	20.55	3
A35	9.98	1	B35	19.55	3
A36	9.32	1	B36	18.6	3
A37	7.97	1	B37	9.56	2
A38	9.55	1	B38	9.2	2
A39	1.66	0	B39	10.66	2
A40	8.08	1	B40	12.66	2
A41	10.7	1	B41	15.5	2
A42	8	1	B42	6.55	1
A43	7.59	1	B43	21.5	3
A44	8.1	1	B44	22.1	3
A45	6.37	1	B45	18.7	3
A46	18.5	3	B46	11.6	2
A47	19.55	3	B47	10.98	2
A48	18.77	3	B48	9.8	2
A49	20.55	3	B49	9.86	2
A50	19.55	3	B50	10.5	2
A51	18.6	3	B51	11.23	2
A52	9.56	2	B52	14.56	2
A53	9.2	2	B53	20.5	3
A54	10.66	2	B54	19.8	3
A55	12.66	2	B55	21.9	3
A56	15.5	2	B56	19.25	3
A57	6.55	1	B57	18.55	3
A58	21.5	3	B58	19.56	3
A59	22.1	3	B59	21.55	3
A60	18.7	3	B60	19.88	3
MEAN ±SD	**6.85±2.6877**	**0.88**	**MEAN±SD**	**14.76±4.1451**	**2.25**
P value - < 0.0001			***** Very highly Significant by Student T Test**		

Radiation-Induced Acute Skin Reactions Evaluated with RTOG Scale:

Table 29 shows that in Group A, the number of patients in Grade 0, 1, 2, 3, 4 were 7(12%), 53(88%), 0, 0, 0 respectively. In Group B, the number of patients in Grade 0, 1, 2, 3, 4 were 0, 3(5%), 39(65%), 18(30%), 0 respectively. This result shows that about 30% of the patients in control had toxicity grade 3 whereas in group treated with Amrad cream has the toxicity scores only in grade 0 and 1.

Table 29: Toxicity grading for skin reactions

TOXICITY GRADING	GROUP A		GROUP B	
	No. of patients	% of patients	No. of patients	% of patients
GRADE 0	7	12	0	0
GRADE 1	53	88	3	5
GRADE 2	0	0	39	65
GRADE 3	0	0	18	30
GRADE 4	0	0	0	0

Adverse events:

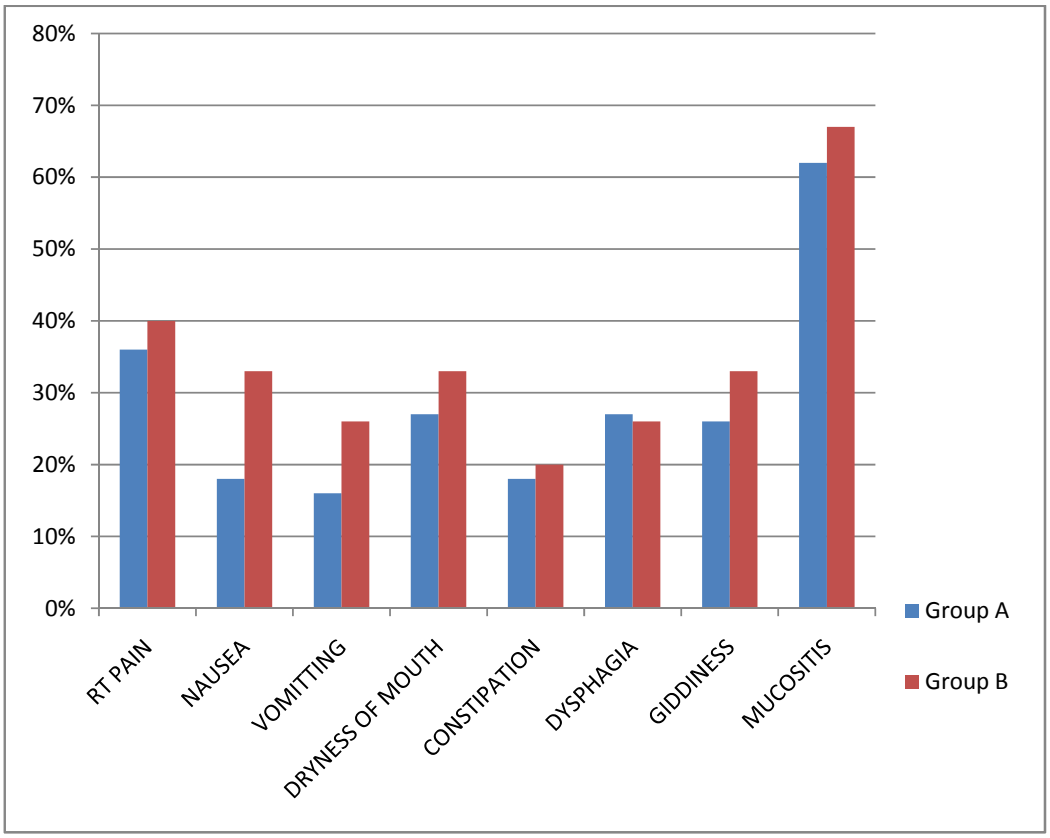
Figure 27 and Table 30 show the presence of adverse events in Group A and Group B patients. The adverse events analysis reveals that in Group A, 36% of patients had RT pain, 18% of patients had nausea, 16% of patients had vomitting, 27% of patients had mouth dryness, 18% of patients had constipation, 27% of patients had dysphagia, 26% of patients had giddiness and 62% of patients had mucositis. In Group B, 40% of patients had RT pain, 33% of patients had nausea, 26% of patients had vomitting, 33% of patients had mouth dryness, 20% of patients had constipation, 26% of patients had dysphagia, 33% of patients had giddiness and 67% of patients had mucositis.

Table: 30
ADVERSE DRUG EVENTS FOR GROUP A (AMRAD CREAM) AND GROUP B (CONTROL)

ADVERSE DRUG REACTION	GROUP A	GROUP B
RT PAIN	36%	40%
NAUSEA	18%	33%
VOMITTING	16%	26%
DRYNESS OF MOUTH	27%	33%
CONSTIPATION	18%	20%
DYSPHAGIA	27%	26%
GIDDINESS	26%	33%
MUCOSITIS	62%	67%

Figure 27

ADVERSE DRUG EVENTS FOR GROUP A (AMRAD CREAM) AND GROUP B (CONTROL)



Patient education:

Table 31 indicates the impact of patient education (counseling) of patient knowledge about cancer, radiotherapy treatment side effects, treatment of radiation induced skin complications, medication usage and storage and dietary counseling. It clearly indicates that patient knowledge of the above mentioned factors have been improved after patient education (counseling). It shows the importance of patient counseling to improve the therapeutic outcomes and quality of life of the patients. Further it confirms that patient counseling can improve the patient compliance and adherence to therapy.

Table : 31

PATIENT EDUCATION FORM

Questions	Before patient education	After patient education	Percentage of improved patient knowledge
1) Do you know about cancer?			
a) Yes	99 (82%)	120 (100%)	100%
b) No	21 (18%)		
If yes, what do you know about cancer?			
a) Malignant tumor	44 (45%)		
b) Benign tumor	21 (22%)		89%
c) **Malignant tumor and Metastasis**	23 (24%)	11 (9%)	
d) Others	9 (9%)	109 (91%)	
2) What are the social habits that cause cancers?			
a) Tobacco use	12 (12%)		
b) Betel nut use	19(18%)		
c) Alcohol use	14(13%)		97%
d) Smoking	27(26%)	12 (10%)	
e) All	33(31%)	108(90%)	
3) Do you have any of these social habits?			
a) Yes	87 (72%)	9 (7%)	92.5%
b) No	33 (28%)	111 (93%)	
4) What are the treatments available for cancers?			
a) Radiotherapy	52 (43%)		
b) Chemotherapy	28 (23%)	120 (100%)	100%
c) Surgery	33 (28%)		
d) Combination of any of the above (a/b/c)	7 (6%)		

5) Do you know about the Radiotherapy treatment? **a) Yes** b) No	 92 (77%) 28 (23%)	 120 (100%)	 100 %
6) Do you know that you have to attend the radiotherapy regularly as per doctor's advice? **a) Yes** b) No	 102 (85%) 18 (15%)	 120 (100%)	 100%
7) Do you know that radiotherapy interruption would delay up the effectiveness of your treatment? **a) Yes** b) No	 44 (37%) 76 (63%)	 120 (100%)	 100%
8) Are you aware of the side effects of the Radiotherapy treatment? **a) Yes** b) No If yes, who told you? a) Doctor b) Pharmacist c) Nurse d) Others	 22 (18%) 98 (82%) 13 (59%) 9 (41%)	 109 (91%) 11(9%) -	 91%
9) Do you know that Radio dermatitis one of the side effects of the radiotherapy treatment? **a) Yes** b) No	 23 (19%) 97 (81%)	 120 (100%)	 100%

10) How will you manage the Radio dermatitis? a) By applying oil. b) **By applying Amrad cream**. c) By informing doctor d) None	 44 (37%) 12(10%) 47(39%) 17(14%)	 21 (17%) 67(56%) 32 (27%) -	NA
11) Do you have any problems with the Amrad cream? a) Yes b) **No**	 7 (12%) 52 (88%)	60 (100%)	100%
12) Where do you store your medicine? a) Refrigerator **b) At room temperature** c) Others	 54 (90%) 6 (10%)	60 (100%)	100%
13) Do you know how to use this medicine? **a) Yes** b) No	 56 (93%) 4 (7%)	60 (100%)	100%
14) Do you know when to apply this medication? **a) Morning and night** b) Night c) Evening d) At any time	 21 (33%) 19 (30%) 0 23 (37%)	60 (100%)	100 %

15) If you find any side effects while taking the medication what will you do? **a) I will inform to the doctor** b) I will skip the medication c) I don't know d) I will chose alternative myself	37 (72%) 9 (18%) 3 (6%) 2 (4%)	57 (95%) 3 (5%)	89%
16) Do you have faith that your treatment would cure the disease? **a) Yes I have faith** b) No I don't have	71 (59%) 49 (41%)	111 (92%) 9(8%)	92.5%
17) Are you following the doctor's advice? **a) Yes** b) No	87 (72%) 33(28%)	120 (100%)	100%
18) Are you following the dietary instructions such as taking rich fruit juices, soft foods and avoiding hot spicy foods properly? **a) Yes** b) No	69 (57%) 51 (43%)	120 (100%)	100%
19) Are you applying the Medication regularly? **a) Yes** b) No	52 (87%) 8 (13%)	60 (100%)	100%
20) Do you check the expiry date while purchasing the medication? **a) Yes** b) No	57(95%) 3(5%)	60 (100%)	100%

21) Do you think that the benefit supersede the cost of the treatment? **a) Yes** b) No	51 (88%) 7(12%)	-	NA
22) Do you know that there is greater chance of recurrence of cancers and that regular follow-up visit is vital **a) Yes** b) No	67 (56%) 53 (44%)	120 (100%)	100%

9. DISCUSSION

The demographics in this study reveal that the risk of developing cancer increases with age. The results show that 59% of patients were in the age group between 50 - 59 who were affected with radiodermatitis. Further in the population under study, 65% were female and 35% were male. This clearly shows that predominantly women get affected more than men.

In most cases the cause of cancer is multifactorial. About 75% of cancers are due to environmental factors and some are due to individuals, e.g tobacco chewing, smoking etc **(Bennett P.N et al., 1996).**

Among the 120 patients entered into the study, 41 patients were found to be affected with cervical carcinoma. According to this report, most of the women were diagnosed with cervical cancer comparing to other cancers. Patients involved in this study group were mostly with curative moderately differentiated tumours and the amount of tumour dose used was 50gy.

The comparative data's in this study reveals that there is a remarkable changes in the radiation-induced skin complications such as erythema, Epilation, edema, pain, desquamation, pigmentation changes, telangiectasia and ulceration. This study paves a way to decrease the rate of skin complications by applying the herbal cream Amrad.

- **Erythema:**

  The comparative data shows that the herbal cream has reduced the erythematic condition of the patients in Group A (Amrad treated group) than the patients in Group B (untreated control group). Erythema is caused due to the release of cytokines that leads to leukocyte infiltration and localized swelling.

- **Epilation:**

  Aloe vera is used to treat epilation conditions (**Zawahry M. *et al.*, 1973).** It is reported that the "complete regeneration of skin of the forehead and scalp, new hair growth, complete restoration of sensation, and absence of scars **(C. E. and Creston Collinset al., 1935).** It reduces the condition of epilation which is caused due to the damage of sebaceous glands and hair follicles in the dermal layer. This clearly reveals that the skin toxicity is less in group of patients treated with Amrad cream.

- **Pain:**

  Radiotherapy induced pain occurred in most of the cancer patients during their treatment period (**Robert H. Davis *et al.,*** in **1988)**. The results show that the severity of pain in Group A patients is less than that of Group B.

- **Edema:**

  Edema which is characterized by the accumulation of the excessive watery fluids in the cells/tissues is also one of the skin complications during radiation therapy (**J.E. (MD) *et al.*, 1937)**. In this study, the patients in group A had decreased condition of edema than the Group B.

- **Desquamation:**

  The condition of desquamation characterized by dryness, scaling and purities (**Cole *et al.,*** in **1935)** has been reduced in group A patients than the patients in group B.

- **Pigmentaton changes:**

  Pigmentaton changes due to the destroyed dermal melanocyte is seen to be reduced in the group A patients than the patients in group B.

- **Telangiectasia:**

  Telangiectasia characterized by the prominent, dilated, thin blood vessels (**Carroll. S .Wright M.D *et al.,*** in **1936)** has been reduced in the group A patients than the patients in group B.

- **Ulceration:**

  C. C. Lushbaugh M.D *et al.,* in **1953** concluded in his study that A. Vera contains substances that are stimulatory both to the relayed development and delayed healing of ulcerative radio dermatitis. Ulceration has been reduced in the group A patients than the patients in group B.

- **Cumulative score:**

  The mean and standard deviation for the overall score for all the parameters among Group A (Amrad) were compared with that of Group B (Control) and it is calculated .The toxicity evaluation grading shows that there is a remarkable decline in the severity of symptoms in the treated group (Group A) when compared to control group (Group B). The mean toxicity grade is higher in Group B than Group A.

  No grade 2 or 3 maximum is seen in the group A. Thus the treated group (Group A) is showing a good protection against radiation induced skin complications than the control group (Group B).

ADR

The presence of adverse events in Group A and Group B patients was studies. The adverse events were analyzed for RT pain, nausea, vomiting, mouth dryness, constipation, dysphagia, giddiness. The data shows a protective effect was seen in the Amrad group than the control group.

PATIENT EDUCATION

The impact of patient education (counseling) had shown significant improvement on patient knowledge about cancer, radiotherapy treatment side effects, treatment of gastro intestinal complications, medication usage and storage; and dietary counseling. The added advantage of the counseling was perhaps due to the fact that it was made in local vernacular.

CONCLUSION

This study concludes thus:

- Age group of 50-59 is highly at risk for cancer.
- Females are affected more than males.
- Smoking and tobacco chewing are the definitive risk factors.
- Cervix and breast cancer are the most prevalent types in women and oesophagus and larynx in men.
- Most of the tumours are moderately differentiated.
- All cumulative scores for skin reaction parameters clearly reveal that there is a desirable effect produced by Amrad cream in group A as compared to group B.
- The final conclusion of the toxicity study shows that radiation induced acute skin reactions of grade 2 and grade 3 are seen in the control group whereas the Amrad treated group does not show the toxicity of grade 2 or above.
- The ADR effects are found to be mild in the herbal cream group A compared to the control group B.
- Patient counseling has improved the patient's knowledge about cancer and radio dermatitis problems, its drug usage and the patient compliance.

Hence we conclude that Amrad is safe and effective in reducing the incidence of radio dermatitis in cancer patients undergoing radiotherapy and also it reduces the severity of grade 2 toxicity in these patients.

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PROFORMA – I

INFORMED CONSENT FORM

Patient Name: **Date:**

Age: **Sex:**

I was explained about the description of the research study and they have answered all the questions I have at this time.

I freely volunteer to participate in this study. I understand that I need not have to take part in this study and that my refusal to participate will involve no penalty. Further I understand that I am free to discontinue participation from this study at any time.

Clinician's Name: **Patient's name:**

Signature:

PROFORMA – II

PATIENT DETAILS FORM

Patient's Name	**:**	**RT NO**	**:**
Age	**:**	**TR NO**	**:**
Sex	**:**	**HR NO**	**:**
Address	**:**		
Ph.No	**:**		
Weight	**:**		
Height	**:**		
Occupation	**:**		
Date of first consultation	**:**		
Reason for Admission	**:**		
Social History	**:**	**a)Smoker b)Alcoholic c)Vegetarian d)Non vegetarian e)Tobacco f)None**	
Past Medical History	**:**		
Diagnosis	**:**		
Surgery/ Radiation	**:**		
History of present illness	**:**		

PROFORMA – III

RADIATION (RT) DETAILS

Patient name :

Radiotherapy type : **Teletherapy**

Site treated :

Total tumor dose prescribed :

Treatment duration :

Total no. of fractions prescribed :

Daily tumor dose :

RADIATION CHART

Radiation Date	Day	Daily surface dose (Gy)	Total surface dose (Gy)	Daily tumour dose (Gy)	Total tumour dose (Gy)

PROFORMA – IV

INVESTIGATIONAL PARAMETERS

Review	Erythema	Epilation	Edema	Desquamation	Pigmentation changes	Telangiectasis	Pain	Ulceration

PROFORMA- V

WHO SKIN TOXICITY ASSESSMENT SCALE

WHO TOXICITY ASSESSMENT SCALE	
TOTAL SCORE	**TOXICITY EVALUATION GRADINGS**
0-2	**0**
3-9	**1**
10-18	**2**
19-27	**3**
28-36	**4**

PROFORMA-VI

ADVERSE DRUG EFFECTS FORM

Weeks	Pain	Nausea	Itching	Mouth Dryness	Dysphagia	Giddiness	Mucositis
Week-1							
Week-2							
Week-3							
Week-4							
Week-5							
Week-6							

PROFORMA – VII

PATIENT EDUCATION FORM

1) Do you know about cancer?

a) Yes b) No

If yes, what do you know about cancer?

a) Malignant tumor b) Benign tumor

c) Malignant and metastasis d) others

2) Do you have any of these social habits?

a) Tobacco b) Alcoholic

c) Smoking d) None

3) Do you have any of these social habits?

a) Yes b) No

4) What are the treatments available for cancer?

a) Radiotherapy b) Chemotherapy

c) Surgery d) Combination of any of the above (a/b/c)

5) Do you know about the Radiotherapy treatment?

a) Yes b) No

6) Do you know that you have to attend the radiotherapy regularly as per doctor's advice?

a) Yes b) No

7) Do you know that radiotherapy interruption would delay up the effectiveness of your treatment?

a) Yes b) No

8) Are you aware of the side effects of the Radiotherapy treatment?

a) Yes b) No

If yes, who told you?

a) Doctor b) Pharmacist

c) Nurse d) Others

9) Do you know that Skin Dermatitis is one of the side effects of the radiotherapy treatment?

a) Yes b) No

10) How will you manage the Skin Toxicities during radiation?

a) By applying oil over the skin.

b) By consulting doctor

c) By using Amrad cream

d) I didn't follow any of these measures

11) Do you have any problems with Amrad cream?

a) Yes b) No

12) Where do you store your medicine?

a) Refrigerator b) At room temperature c) Anywhere

13) Do you know how to use this cream?

a) Yes b) No

14) Do you know when to apply this cream?

a) Morning b) Night

c) Before radiation d) at any time

15) If you find any side effects while using this cream what will you do?

a) I will inform to the doctor

b) I will stop the medication

c) I don't know

d) I will choose alternative myself

16) Do you have faith that your treatment would cure the disease?

a) Yes I have faith b) No I don't have

17) Are you following the doctor's advice?

a) Yes b) No

18) Are you following the dietary instructions such as taking rich fruit juices, soft foods and avoiding hot spicy foods properly?

a) Yes b) No

19) Are you applying the Medication regularly?

a) Yes b) No

20) Do you check the expiry date while purchasing the medication?

a) Yes b) No

21) Do you think that the benefit supersede the cost of the treatment?

a) Yes b) No

22) Do you know that there is greater chance of recurrence of cancers and that regular follow-up visit is vital?

a) Yes b) No